Baskar
09/900575

(FILE 'HCAPLUS' ENTERED AT 15:24:35 ON 03 DEC 2002)
L1 135 SEA FILE=HCAPLUS ABB=ON PLU=ON ((ENTEROBACILL? OR ENTERO BACILL?)(5A)(DISEAS? OR DISORDER) OR UTI OR (UT OR URINARY TRACT OR BLADDER)(W)INFECT?) AND ADHESIN
L2 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND (MOAB OR MAB OR ANTIBOD?)

-key terms

L2 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:830177 HCAPLUS
DOCUMENT NUMBER: 137:324219
TITLE: Type 1 and type P fimbriae-**adhesins** isolated from novel E. coli strains, process for their preparation and uses thereof for immunization against **urinary tract infections**
INVENTOR(S): Palacios Pelaez, Ricardo; Martinez Garate, Alberto; Martinez Quesada, Jorge
PATENT ASSIGNEE(S): Industrial Farmaceutica y de Especialidades, S.A., Spain
SOURCE: U.S., 13 pp., Cont.-in-part of U.S. Ser. No. 858,903, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6471966	B1	20021029	US 1998-128484	19980804
ES 2076895	A1	19951101	ES 1994-202	19940204
ES 2076895	B1	19960816		

PRIORITY APPLN. INFO.: ES 1994-202 A 19940204
US 1995-383765 B1 19950203
US 1997-858903 B2 19970519

AB Fimbriae **adhesins** have a mol. wt. of 2.times.105 and 2.times.107 Da, and are comprised of 90-95% protein and 1-3% sugar. Type 1 fimbriae include 5 different protein fractions of 14-20 kDa, most of which are assocd. with carbohydrates. Type P fimbriae also include 5 different protein fractions of 14-20 kDa, and one of the majority proteins is assocd. with carbohydrates. The process of the invention comprises: culturing E. coli strains CECT 4484 and CECT 4485; collecting the sediment by centrifugation and resuspending it in physiol. saline followed by homogenization; centrifuging the homogenate and collecting the supernatant; pptg. the supernatant with saline, reconstituting the ppt. and dialyzing the soln.; treating the dialyzate with sodium deoxycholate and, subjecting the product to two successive chromatogs. with Sephacryl S-200 and Sepharose 4B. The product is used for treatment and prevention of infections of the urinary tract caused by fimbriated E. coli.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:505237 HCAPLUS
DOCUMENT NUMBER: 137:62166
TITLE: Engineered pilus proteins for vaccination and

immunotherapy

INVENTOR(S): Hultgren, Scott J.; Langermann, Solomon; Sauer, Frederic G.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002086037	A1	20020704	US 2001-27350	20011228
WO 2002059156	A2	20020801	WO 2001-US51037	20011220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-257880P P 20001222

AB The authors disclose construction of pilus proteins exhibiting structural stabilization. Stabilization is achieved by occupation of the subunit-binding site by a covalently attached N-terminal extension domain or non-covalently by an engineered chaperone or other pilus protein. Such extension provides a "donor strand complementary" segment which may be altered to attach an auxiliary portion.

L2 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:504804 HCAPLUS

DOCUMENT NUMBER: 137:77872

TITLE: Synthetic peptide immunogens for prevention of **urinary tract infection**

INVENTOR(S): Wang, Chang Yi

PATENT ASSIGNEE(S): United Biomedical Inc., USA

SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051860	A2	20020704	WO 2001-US50816	20011221

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,

TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-747802 A 20001222

AB The invention provides peptide immunogens comprising a FimH **adhesin**-derived peptide, or an analog thereof, covalently linked to a helper T cell epitope and optionally to an invasin immunostimulatory domain. The present invention also provides for the use of such peptide immunogens to elicit the prodn. in mammals of high titer polyclonal **antibodies**, which are specific to the FAFSD target peptide. The peptide immunogens are expected to be useful in evoking **antibodies** that prevent the adherence of Escherichia coli and other enterobacteria to the bladder mucosa.

L2 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:51508 HCAPLUS
DOCUMENT NUMBER: 136:117368
TITLE: FimH **adhesins** of Escherichia coli for therapy of **urinary tract infections**
INVENTOR(S): Langermann, Solomon; Revel, Andrew; Auguste, Christine; Burlein, Jeanne
PATENT ASSIGNEE(S): Medimmune, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004496	A2	20020117	WO 2001-US21525	20010706

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002150587	A1	20021017	US 2001-900575	20010706

PRIORITY APPLN. INFO.: US 2000-216750P P 20000707

AB The authors disclose the sequence characterization and recombinant expression of variants of the E. coli FimH protein. A plasmid-based method of producing FimH **adhesins** and FimC-FimH complexes are also disclosed. The recombinant **adhesins** are suggested for vaccination against **urinary tract infections**.

L2 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:197347 HCAPLUS

TITLE: Functional Pilus-Specific Vaccine-Induced **Antibodies** for **Urinary Tract Infections**
AUTHOR(S): Jian, L.; Fusco, P. C.
CORPORATE SOURCE: Baxter Healthcare Corporation, Columbia, MD, 21046, USA
SOURCE: Abstr. Pap. - Am. Chem. Soc. (2001), 221st, BIOT-040
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English

AB Pilus-assocd. tip **adhesins** have been pursued as vaccine candidates, particularly for uropathogenic Escherichia coli. Pili are polymers of identical pilin proteins, forming rods at the cell surface, which may contain sep. tip **adhesin** proteins for binding to eukaryotic receptors. P pilus vaccines have previously protected against **urinary tract infections** in mouse models, where digalactosyl receptors occur throughout the urinary tract. We are examg. the role of P pili in eliciting functionally active **antibodies** that block attachment to receptors, independent of tip **adhesins**. Blocking attachment of purified pili to receptors on human erythrocyte ghosts was investigated using an inhibition ELISA-based method. An inhibition agglutination assay was also employed for measuring inhibition of piliated bacteria attachment to receptors on human erythrocyte ghosts and digalactosyl-latex beads, using pilus-specific rabbit antisera, purified IgG, and Fab fragments. One of several P pilus serotypes, F71, was used for binding to human erythrocyte ghosts on microtiter plates, and pilus-specific antiserum detected this binding by ELISA. Homologous (F71) and heterologous (F72, F9, F13) antisera, against pili with different **adhesins** (class I or II), were titrated and mixed with pili to competitively inhibit binding, giving 50% inhibition titers of 6400 and 800-1600, resp. In addn., heterologous monoclonal **antibody** against F13 P pili with a different **adhesin** inhibited F71 pilus binding by 52%. Inhibition occurred independently of **adhesins** since: (1) heterologous antiserum for pili with a class I **adhesin** inhibited pili with a different class II **adhesin**, and (2) pilin-specific monoclonal **antibodies** inhibited pilus binding. Homologous and heterologous inhibition of bacterial attachment was also demonstrated with pilus-specific antisera, yielding inhibition titers for digalactosyl-latex beads that were 8-16 and 1-8 times higher, resp., than with neg. control sera. Homologous antiserum gave an inhibition titer of 38,400 in preventing bacterial agglutination of human erythrocyte ghosts. To demonstrate blocking of attachment independent of agglutination, Fab fragments were produced which completely inhibited bacterial agglutination of digalactosyl-latex beads at 33 .mu.g/mL. Purified pilus vaccines can therefore elicit **antibodies** that block attachment of bacteria and their pili to host cells independent of tip **adhesins**.

L2 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:64163 HCAPLUS
DOCUMENT NUMBER: 134:130261
TITLE: Escherichia coli FimH **adhesin** peptides

and fusion proteins, and their use as vaccines for preventing diseases such as **urinary tract infection**

INVENTOR(S): Hultgren, Scott J.; Langermann, Solomon
PATENT ASSIGNEE(S): Medimmune, Inc., USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005978	A1	20010125	WO 2000-US19402	20000714
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194563	A1	20020410	EP 2000-950385	20000714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-144016P P 19990715
WO 2000-US19402 W 20000714

AB The invention provides immunogenic polypeptides comprising one or more domains of the Escherichia coli gene fimH **adhesin** protein, wherein the domains include mannose-binding (MBD) or collagen-binding (COL) domains. Five specific FimH polypeptides are provided including: (1) MBD-1, MBD-2 and MBD-3, which contain mannose-binding domains; (2) COL, which contains the collagen-binding domain, and (3) MBD-C which contains mannose and collagen binding domains. The invention also provides immunogenic FimH fusion proteins comprising said polypeptides sepd. by a linker peptide contg. glycine and serine amino acids. The invention specifically provides three fusion proteins including: (1) MBD-1-MBD-2-MBD-3; (2) MBD-1-MBD-C-MBD-3 and (3) MBD-1-MBD-2-COL-MBD-3. The invention further provides: (1) polynucleotides encoding the various FimH domains; (2) monoclonal **antibodies** specific for the said FimH polypeptides and fusion proteins; and (3) compn. comprising said monoclonal **antibody**. Still further, the invention provides for the use of said FimH polypeptides and fusion proteins as vaccines for preventing diseases caused by E. coli in humans, such as **urinary tract infection**. The amino acid sequences of E. coli MBD-1, MBD-2 and MBD-3 peptides are provided. The invention also included amino acid sequences of the fusion proteins claimed.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:597324 HCAPLUS

DOCUMENT NUMBER: 127:277150
TITLE: Localization of a domain in the FimH **adhesin** of Escherichia coli type 1 fimbriae capable of receptor recognition and use of a domain-specific **antibody** to confer protection against experimental **urinary tract infection**
AUTHOR(S): Thankavel, Krishnan; Madison, Bereneice; Ikeda, Teruo; Malaviya, Ravi; Shah, Ankur H.; Arumugam, Prabhu M.; Abraham, Soman N.
CORPORATE SOURCE: Department of Pathology, Barnes-Jewish Hospital, St. Louis, MO, 63110, USA
SOURCE: Journal of Clinical Investigation (1997), 100(5), 1123-1136
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The FimH subunit of type 1-fimbriated Escherichia coli has been implicated as an important determinant of bacterial adherence and colonization of the urinary tract. Here, we sought to localize the functionally important domain(s) within the FimH mol. and to det. if **antibodies** against this domain would block adherence of type 1-fimbriated E. coli to the bladder mucosa in situ and in vivo in an established mouse model of cystitis. We generated translational fusion proteins of disparate regions of the FimH mol. with an affinity tag MalE, and tested each of the fusion products in vitro for functional activity. The min. region responsible for binding mouse bladder epithelial cells and a sol. mannoprotein, horseradish peroxidase, was contained within residues 1-100 of the FimH mol. We validated and extended these findings by demonstrating that **antibodies** directed at the putative binding region of FimH or at synthetic peptides corresponding to epitopes within the binding domain could specifically block type 1 fimbriae-mediated bacterial adherence to bladder epithelial cells in situ and yeast cells in vitro. Next, we compared the ability of mice passively immunized i.p. with antisera raised against residues 1-25 and 253-264 of FimH or 1-13 of FimA to resist bladder colonization in vivo after intravesicular challenge with type 1-fimbriated E. coli. Only the **antibody** directed at the putative binding region of FimH (anti-s-FimH1-25) significantly reduced E. coli **bladder infections** in the exptl. mouse model of **urinary tract infections**. Similar results were obtained when the mice were actively immunized with synthetic peptides corresponding to residues 1-25 and 253-264 of FimH or 1-13 of FimA. The mechanism of protection was attributed, at least in part, to inhibition of bacterial adherence to the bladder surface by s-FimH1-25-specific **antibody** mols. that had filtered through the kidneys into the urine. The level of **antibodies** entering the bladder from the circulatory system of the immunized mice was found to be markedly enhanced upon bacterial challenge. The potential broad spectrum activity protective FimH **antibody** was indicated from its serol. cross-reactivity with various urinary tract bacterial is bearing type 1 fimbriae. These findings could be rele design of an efficacious and broadly reactive FimH va **urinary tract infections**.

Searcher : Shears 308-4994

L2 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:376629 HCAPLUS
DOCUMENT NUMBER: 127:106513
TITLE: Occurrence of S and F1C/S-related fimbrial determinants and their expression in Escherichia coli strains isolated from extraintestinal infections
AUTHOR(S): Sokolowska-Koehler, Wanda; Schoenian, Gabriele; Bollmann, Renate; Schubert, Andre; Parschau, Jana; Seeberg, Anke; Presber, Wolfgang
CORPORATE SOURCE: Institut fuer Mikrobiologie und Hygiene, Universitaetsklinikum Charite, Humboldt-Universitaet Berlin, Dorotheenstr. 96, Berlin, D-10098, Germany
SOURCE: FEMS Immunology and Medical Microbiology (1997), 18(1), 1-6
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The presence of S and F1C/S-related fimbrial determinants was detd. in 462 E. coli strains obtained from different extraintestinal infections and in 162 control isolates of E. coli by using two different DNA probes: an oligonucleotide probe consisting of three oligonucleotides that bind specifically to the S **adhesin** gene and a polynucleotide probe which is not able to distinguish between S, F1C, and S-related sequences. The expression of S and F1C phenotypes was tested by dot enzyme immunoassay with the corresponding monoclonal **antibodies**. S fimbriae genotypes were obsd. more frequently in septic (25%) and urinary (12%) isolates of E. coli than in faecal and water isolates (1%) and often occurred together with O2, O6, O18 and O83 antigens. F1C/S-related fimbrial DNA was detected with a higher frequency in **UTI** isolates (26%) than in septic (16%) and faecal (10%) isolates and was most frequently assocd. with O4, O6, and O75 serotypes. Since the prodn. of S and F1C fimbriae was comparatively rare in all clin. and control isolates of E. coli, DNA hybridization assays which allow the sensitive and specific detection of fimbrial determinants even in the absence of their expression are preferable to phenotypic assays.

L2 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:522514 HCAPLUS
DOCUMENT NUMBER: 122:287885
TITLE: dra-Related X **adhesins** of gestational pyelonephritis-associated Escherichia coli recognize SCR-3 and SCR-4 domains of recombinant decay-accelerating factor
AUTHOR(S): Pham, Tuan; Kaul, Anil; Hart, Audrey; Goluszko, Pawel; Moulds, John; Nowicki, Stella; Lublin, Douglas M.; Nowicki, Bogdan J.
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. Texas, Galveston, TX, 77555, USA
SOURCE: Infection and Immunity (1995), 63(5), 1663-8
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Bacterial **adhesins** are important virulence factors that allow colonization of the human urogenital tract by Escherichia coli. **Adhesins** of the Dr family have been found to be more frequently expressed in strains assocd. with symptomatic **urinary tract infections**. Because of the high frequency of symptomatic **urinary tract infections** during pregnancy, we screened E. coli isolates from 64 gestational pyelonephritis patients for the expression of Dr and X **adhesins** to address their potential virulence roles in this population. Using PCR and primers for the afaB gene, we detected dra-related operons in 17 isolates (27%). On the basis of the lack of hemagglutination of Dr(a-) erythrocytes contg. a point mutation in the decay-accelerating factor (DAF) short consensus repeat-3 (SCR-3) domain, 12 of these strains were categorized as classical Dr **adhesins**. The hemagglutination of O erythrocytes by Dr+ strains was blocked or reduced by a monoclonal **antibody** to the DAF SCR-3 domain. The remaining five dra-pos. strains agglutinated Dr(a-) erythrocytes. Monoclonal **antibody** to the DAF SCR-3 domain failed to block O-erythrocyte hemagglutination. **Adhesins** in these strains did not fulfill criteria for Dr hemagglutinins because of the undefined receptor specificities and were categorized as X. E. coli strains bearing dra-related X **adhesins** bound to DAF cDNA-transfected Chinese hamster ovary cells. Three of these dra-related X-**adhesin**-bearing E. coli strains failed to attach to the SCR-3.DELTA. deletion transfectant, which suggested that binding sites were located in the SCR-3 domain but outside the region blocked by the monoclonal anti-SCR-3 IgG. The binding sites of the remaining two dra-related X **adhesin** strains were localized to the SCR-4 domain, as the attachment was shown to be abolished on an SCR-4.DELTA. mutant but unaffected by an SCR-3.DELTA. deletion. The heterogeneity in the binding sites of E. coli DAF (Dr) family **adhesins** from gestational pyelonephritis isolates may reflect the ability of the **adhesins** to evolve to recognize alternate peptide epitopes for efficient colonization.

L2 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:507438 HCAPLUS

DOCUMENT NUMBER: 122:312013

TITLE: Glycoconjugate receptors for P-fimbriated Escherichia coli in the mouse. An animal model of **urinary tract infection**

AUTHOR(S): Lanne, Boel; Olsson, Britt-Marie; Jovall, Per-Aake; Aangstroem, Jonas; Linder, Henrik; Marklund, Britt-Inger; Bergstroem, Joergen; Karlsson, Karl-Anders

CORPORATE SOURCE: Dep. Med. Biochem., Goeteborg Univ., Goeteborg, S-413 90, Swed.

SOURCE: Journal of Biological Chemistry (1995), 270(15), 9017-25
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Glycosphingolipids were isolated from kidneys, urethers, and bladders (including urethrae) of C3H/HeN mice. Binding was studied of a clin. isolate and recombinant strains of uropathogenic P-fimbriated Escherichia coli to these glycolipids. A series of receptor-active glycolipids with Gal.alpha.4Gal in common, previously shown to be recognized by these bacteria, was identified by use of specific monoclonal **antibodies**, fast-atom bombardment and electron-impact mass spectrometry, and proton NMR spectroscopy: galabiosylceramide (Gal.alpha.4Gal.beta.Cer), globotriaoxylceramide (Gal.alpha.4Gal.beta.4Glc.beta.Cer), globoside (GalNAc.beta.3Gal.alpha.4Gal.beta.4Glc.beta.Cer), the Forssman glycolipid (GalNAc.alpha.3GalNAc.beta.3Gal.alpha.4Gal.beta.4Glc.beta.Cer), Gal.beta.4GlcNAc.beta.6(Gal.beta.3)GalNAc.beta.3Gal.alpha.4Gal.beta.4Glc.beta.Cer, and Gal.beta.4(Fuc.alpha.3)GlcNAc.beta.6(Gal.beta.3)GalNAc.beta.3Gal.alpha.4Gal.beta.4Glc.beta.Cer. The binding pattern for mouse kidney glycolipids differed from that for kidney glycolipids of man and monkey. In particular, the dominant 8-sugar glycolipid in the mouse was not detected in the primates. A second difference was found in the binding of E. coli to kidney glycoproteins on blots after electrophoresis; the mouse showed distinct receptor-active bands while human and monkey did not. These differences may be of relevance when using the mouse as a model for clin. **urinary tract infection** of man.

L2 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:631948 HCAPLUS
DOCUMENT NUMBER: 117:231948
TITLE: Binding of uropathogenic Escherichia coli R45 to glycolipids extracted from vaginal epithelial cells is dependent on histo-blood group secretor status
AUTHOR(S): Stapleton, Ann; Nudelman, Edward; Clausen, Henrik; Hakomori, Senitiroh; Stamm, Walter E.
CORPORATE SOURCE: Dep. Med., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Journal of Clinical Investigation (1992), 90(3), 965-72
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Women with a history of recurrent E. coli **urinary tract infections** (**UTIs**) are 2-3 times more likely to be nonsecretors of histo-blood group antigens than are women without such a history. Further, uroepithelial cells from women who are nonsecretors show enhanced adherence of uropathogenic E. coli compared with cells from secretors. To investigate the hypothesis that nonsecretors express unique receptors for uropathogenic E. coli related to their genetic background, the authors extd. glycosphingolipids (GSLs) from vaginal epithelial cells collected from nonsecretors and secretors and used an assay in which radiolabeled uropathogenic E. coli were bound to these GSLs sepd. on TLC plates. An E. coli strain (R45) expressing both P and F **adhesins**, which was isolated from one of these patients' **UTIs**, was metabolically labeled with 35S for the TLC binding assay. The radiolabeled E. coli R45 bound to 2 extended globo-series GSLs, sialosyl gal-globoside (SGG) and disialosyl gal-globoside (DSGG), found in the GSL exts. from nonsecretors but

not from secretors. The identity of SGG in the nonsecretor GSL exts. was confirmed in RIAs using an **mAb** to SGG and in immunofluorescence assays with this **mAb** and native vaginal epithelial cells. SGG and DSGG are selectively expressed by epithelial cells of nonsecretors, presumably as a result of sialylation of the gal-globoside precursor glycolipid, which in secretors is fucosylated and processed to ABH antigens. The presence of SGG and DSGG may account for the increased binding of E. coli to uroepithelial cells from nonsecretors and for their increased susceptibility to recurrent **UTIs**.

L2 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:677798 HCAPLUS
DOCUMENT NUMBER: 115:277798
TITLE: Proteus mirabilis flagella and MR/P fimbriae: isolation, purification, N-terminal analysis, and serum **antibody** response following experimental **urinary tract infection**
AUTHOR(S): Bahrani, Farah K.; Johnson, David E.; Robbins, David; Mobley, Harry L. T.
CORPORATE SOURCE: Sch. Med., Univ. Maryland, Baltimore, MD, 21201, USA
SOURCE: Infection and Immunity (1991), 59(10), 3574-80
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Urinary tract infection** with P. mirabilis may lead to serious complications, including cystitis, acute pyelonephritis, fever, bacteremia, and death. In addn. to the prodn. of hemolysin and the enzyme urease, fimbriae and flagellum-mediated motility have been postulated as virulence factors for this species. Mannose-resistant/proteuslike (MR/P) fimbriae and flagella were purified from strains CFT322 and HU2450, resp. Electron microscopy revealed highly concd. prepns. of fimbriae and flagella. Fimbrial and flagellar structural subunits were estd. by SDS-PAGE to be 18.5 and 41 kDa, resp. N-terminal sequencing revealed that 10 of the first 20 amino acids of the major MR/P subunit matched the sequence of the P. mirabilis uroepithelial cell **adhesin** N-terminus and 11 of 20 amino acids matched the predicted amino acid sequence of the Escherichia coli P fimbriae structural subunit, PapA. In addn., 90 and 80% homologies were found between the first 20 amino acids of P. mirabilis flagellin and those of Salmonella typhimurium phase-1 flagellin and the E. coli hag gene product, resp. An ELISA using purified antigens showed a strong reaction between the MR/P fimbriae or flagella and sera of CBA mice challenged transurethrally with P. mirabilis. A possible role for MR/P fimbriae in the pathogenesis of **urinary tract infection** is supported by (i) a strong immune response to the antigen in exptl. infected animals, (ii) amino acid sequence similarity to other enteric surface structure, and (iii) the previously reported observation that MR/P fimbriae are expressed preferentially as the sole fimbrial type in human pyelonephritis isolates.

L2 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:570495 HCAPLUS
DOCUMENT NUMBER: 113:170495

TITLE: Purification of P-**adhesins** from pathogenic Escherichia coli
INVENTOR(S): Jann, Klaus; Hoschuetzky, Heinz
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3832785	A1	19900419	DE 1988-3832785	19880927

AB The P-adhesions of uropathogenic Escherichia coli are purified for the raising of **antibodies** and for ue in the diagnosis and treatment of **urinary tract infections**.
The complex of fimbriae and **adhesins** are released from the cells by heating or with detergent and the complex cond. by salt pptn. The complex is then solubilized with a zwitterionic detergent, the fimbriae again pptd. with LiCl and the adhesions purified from the supernatant chromatog. Cells of an uropathogenic E. coli were harvested, suspended in isotonic NaCl and heated (65.degree., 30 min) and the cells removed by centrifugation. The supernatant as made 10% satd. in (NH4)2SO4 to ppt. the fimbriae-adhesion complex. After washing and repptn. with LiCl the complex was broken up by heating in the presence of Zwittergent 3-16. The fimbriae were removed by centrifugation and the **adhesins** and the papE and papF gene products purified chromatog. P-adhesion was also recovered from cell walls using octylglucoside as a solubilizing agent.

L2 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:162327 HCAPLUS
DOCUMENT NUMBER: 108:162327
TITLE: Distribution and degree of heterogeneity of the afimbrial-**adhesin**-encoding operon (afa) among uropathogenic Escherichia coli isolates
AUTHOR(S): Labigne-Roussel, Agnes; Falkow, Stanley
CORPORATE SOURCE: Inst. Natl. Sante Rech. Med., Inst. Pasteur, Paris, 75015, Fr.
SOURCE: Infection and Immunity (1988), 56(3), 640-8
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The afimbrial **adhesin** (AFA-I) from a pyelonephritic E. coli isolate (KS52) is a mannose-resistant, P-independent, X-binding **adhesin**, expressed by the afa-1 operon. It is distinct from the E. coli X-binding **adhesins** with M and S specificity.
A total of 138 E. coli isolates belonging to various serotypes, mostly from **urinary tract infections**, were screened for the presence of DNA sequences related to the afa operon and for the expression of an X-**adhesin** able to mediate mannose-resistant hemagglutination (MRHA) and adhesion to uroepithelial cells. Fifteen strains harbored DNA sequences related to the AFA-I-encoding operon, and 13 of them expressed an X-

adhesin. Different DNA segments of the AFA-I-encoding operon were used in Southern expts. to show that only 3 of these clin. isolates contained genetic determinants closely related to those identified in the original afa prototype strain (KS52): presence of the afaA, afaB, afaC, afaD, and afaE genes assocd. with the expression of a 16,000-dalton hemagglutinin-adhesion which strongly cross-reacted with AFA-I-specific **antibodies**. The other E. coli isolates harbored DNA sequences homologous to the afaA, afaB, afaC, and afaD genes, but lacked the sequence corresponding to the **adhesin**-producing gene afaE; Western blots allowed the detection of polypeptides (15,000, 15,500, or 16,000 daltons) in these strains which cross-reacted with variable intensity with **antibodies** raised against the denatured AFA-I protein, but did not cross-react with native AFA-I-specific **antibodies**. DNA cloning expts. from chromosomal DNA of 2 of those strains (A22 and A30) showed that although the AFA-related operon in A22 and A30 strains lacked the AFA-I **adhesin** -encoding gene, they synthesized a functional X-**adhesin**. Thus, strains A22 and A30 encode **adhesins** designated AFA-II and AFA-III, which were cloned on recombinant plasmids pILL72 and pILL61, resp. Southern hybridization expts. and Western blot analyses of the 15 AFA-related strains demonstrate the heterogeneity of the genetic sequences encoding the structural **adhesin** and suggest the bases for the serol. diversity of the AFA **adhesins**.

L2 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1987:14129 HCAPLUS
DOCUMENT NUMBER:	106:14129
TITLE:	Analysis of the genetic determinants coding for the S-fimbrial **adhesin** (sfa) in different Escherichia coli strains causing meningitis or **urinary tract infections**
AUTHOR(S):	Ott, Manfred; Hacker, Joerg; Schmoll, Thomas; Jarchau, Thomas; Korhonen, Timo K.; Goebel, Werner
CORPORATE SOURCE:	Inst. Genet. Mikrobiol., Wuerzburg, D-8700, Fed. Rep. Ger.
SOURCE:	Infection and Immunity (1986), 54(3), 646-53 CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The genetic determinant coding for the S-fimbrial **adhesin** (Sfa), a sialic acid-recognizing pilus frequently found among extraintestinal E. coli isolates has recently been cloned. Fimbriae from the resulting Sfa+ E. coli K-12 clone were isolated, and an Sfa-specific antiserum was prepd. Western blots indicate that S fimbriae isolated from different uropathogenic and meningitis-assocd. E. coli strains, including 083:K1 isolates, were serol. related. The Sfa-specific **antibodies** did not cross-react with P fimbriae, but did cross-react with F1C fimbriae. Further the sfa+ recombinant DNAs and some cloned sfa-flanking regions were used as probes in Southern expts. Chromosomal DNAs isolated from 018:K1 and 083:K1 meningitis strains with and without S fimbriae and from uropathogenic 06:K+ strains were hybridized against these sfa-specific probes. Only one copy of the sfa determinant was identified on the chromosome of these strains. No

sfa-specific sequences were obsd. on the chromosome of E. coli K-12 strains and an O7:K1 isolate. With the exception of small alterations in the sfa-coding region the genetic determinants for S fimbriae were identical in uropathogenic O6:K+ and meningitis O18:K1 and O83:K1 strains. The sfa determinants was also detected on the chromosome of K1 isolates with an Sfa-neg. phenotype, and specific cross-hybridization signals were visible after blotting against F1C-specific DNA. In addn. homol. among the different strains was obsd. in the sfa-flanking regions.

L2 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:623920 HCAPLUS
DOCUMENT NUMBER: 105:223920
TITLE: Binding of purified Escherichia coli O75X **adhesin** to frozen sections of human kidney
AUTHOR(S): Korhonen, Timo K.; Virkola, Ritva; Vaisanen-Rhen, Vuokko; Holthofer, Harry
CORPORATE SOURCE: Dep. Gen. Microbiol., Univ. Helsinki, Helsinki, SF-00280, Finland
SOURCE: FEMS Microbiology Letters (1986), 35(2-3), 313-18
CODEN: FMLED7; ISSN: 0378-1097
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Binding characteristics of the purified E. coli 075X **adhesin** in frozen sections of human kidney were detd., by using **antibodies** raised against the purified antigen and rhodamine-conjugated 2nd **antibodies**. To identify the **adhesin**-binding nephron domains, the same tissue sections were double stained with fluorescein isothiocyanate-conjugated nephron site-specific lectins. At the tubular pole, the 075X **adhesin** bound selectively to the basement membrane of proximal and distal tubules and, with a slightly lower efficiency, of collecting ducts. In the glomerulus, the 075X **adhesin** bound only to the parietal epithelial cells (Bowman's capsule). The purified 075X **adhesin** bound also to exfoliated epithelial cells in human urine. These results suggest that the 075X **adhesin** may contribute to the uropathogenicity of E. coli by binding the bacteria to tissue structures in the human urinary tract.

L2 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:435860 HCAPLUS
DOCUMENT NUMBER: 103:35860
TITLE: Protection against Escherichia coli-induced **urinary tract infections** with hybridoma **antibodies** directed against type 1 fimbriae or complementary D-mannose receptors
AUTHOR(S): Abraham, Soman N.; Babu, Jegdish P.; Giampapa, Chris S.; Hasty, David L.; Simpson, W. Andrew; Beachey, Edwin H.
CORPORATE SOURCE: Veterans Adm. Med. Cent., Memphis, TN, 38104, USA
SOURCE: Infection and Immunity (1985), 48(3), 625-8
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hybridoma **antibodies** directed against quaternary structural epitopes of the type 1 fimbrial **adhesin** of E. coli or against D-mannose, the sugar determinant in the complementary host cell receptor, prevented the attachment of mannose-sensitive E. coli to various eucaryotic cells. Passive i.p. administration of the fimbria-specific or D-mannose-specific **antibodies** protected mice against retrograde colonization with mannose-sensitive E. coli instilled into their urinary bladders. Monoclonal **antibodies** directed against fimbrial subunits rather than quaternary structural epitopes or against N-acetylgalactosamine rather than D-mannose residues lacked protective activity. Thus, bacterial colonization can be blocked or interrupted by **antibodies** directed against either the **adhesin** or the complementary host cell receptor of pathogenic microorganisms.

L2 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:165080 HCAPLUS
DOCUMENT NUMBER: 102:165080
TITLE: Mannose-resistant hemagglutination and P receptor recognition of uropathogenic Escherichia coli isolated from adult patients
AUTHOR(S): Gander, Rita M.; Thomas, Virginia L.; Forland, Marvin
CORPORATE SOURCE: Dep. Microbiol., Univ. Texas Health Sci. Cent., San Antonio, TX, 18284, USA
SOURCE: Journal of Infectious Diseases (1985), 151(3), 508-13
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Adhesins** of 211 strains of uropathogenic E. coli and 19 strains of normal fecal E. coli were characterized by patterns of agglutination with human erythrocytes, Saccharomyces cerevisiae, and horse erythrocytes coated with the P blood-group receptor (P). Mannose-resistant (MR) hemagglutination was significantly assocd. with P agglutination. E. coli Expressing MR and/or P (MR/P) agglutinins concurrently with mannose-sensitive (MS) agglutinins predominated in all clin. categories. The highest percentage of E. coli demonstrating MR/P agglutinins, in the absence of MS agglutinins, was recovered from patients with acute pyelonephritis (35%) compared with percentages of patients with chronic pyelonephritis (13%), asymptomatic bacteriuria (16%), cystitis (11%), and normal fecal control E. coli (11%). Sixty-nine percent of E. coli isolates causing acute pyelonephritis agglutinated P-coated horse erythrocytes compared with only 11% of the fecal isolates. Strains expressing MR/P agglutinins (in the absence of MS agglutinins) isolated from patients with acute pyelonephritis, chronic pyelonephritis, and asymptomatic bacteriuria were significantly assocd. with the presence of **antibody**-coated bacteria in patients' urine sediments, an observation indicative of an immune response assocd. with bacterial invasion of host tissues.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:30:32 ON 03 DEC 2002)
L3 93 S L2
L4 62 DUP REM L3 (31 DUPLICATES REMOVED)

L5 24 S L4 AND (TREAT? OR THERAP? OR PREVENT?)
L6 11 S L4 AND ADMIN?
L7 25 S L5 OR L6

L7 ANSWER 1 OF 25 MEDLINE
ACCESSION NUMBER: 2001285417 MEDLINE
DOCUMENT NUMBER: 21117008 PubMed ID: 11179364
TITLE: Polarized entry of uropathogenic Afa/Dr diffusely adhering Escherichia coli strain IH11128 into human epithelial cells: evidence for alpha5beta1 integrin recognition and subsequent internalization through a pathway involving caveolae and dynamic unstable microtubules.
AUTHOR: Guignot J; Bernet-Camard M F; Pous C; Plancon L; Le Bouguenec C; Servin A L
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale (INSERM), Unite 510, France.
SOURCE: INFECTION AND IMMUNITY, (2001 Mar) 69 (3) 1856-68. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

AB Afa/Dr diffusely adhering Escherichia coli strain IH11128 bacteria basolaterally entered polarized epithelial cells by a CD55- and CD66e-independent mechanism through interaction with the alpha5beta1 integrin and a pathway involving caveolae and dynamic microtubules (MTs). IH11128 invasion within HeLa cells was dramatically decreased after the cells were **treated** with the cholesterol-extracting drug methyl-beta-cyclodextrin or the caveola-disrupting drug filipin. Disassembly of the dynamically unstable MT network by the compound 201-F resulted in a total abolition of IH11128 entry. In apically infected polarized fully differentiated Caco-2/TC7 cells, no IH11128 entry was observed. The entry of bacteria into apically IH11128-infected fully differentiated Caco-2/TC7 cells was greatly enhanced by **treating** cells with Ca2+-free medium supplemented with EGTA, a procedure that disrupts intercellular junctions and thus exposes the basolateral surface to bacteria. Basally infected fully differentiated polarized Caco-2/TC7 cells grown on inverted inserts mounted in chamber culture showed a highly significant level of intracellular IH11128 bacteria compared with cells subjected to the apical route of infection. No expression of CD55 and CD66e, the receptors for the Afa/Dr **adhesins**, was found at the basolateral domains of these cells. Consistent with the hypothesis that a cell-to-cell adhesion molecule acts as a receptor for polarized IH11128 entry, an **antibody** blockade using anti-alpha5beta1 integrin polyclonal **antibody** completely abolished bacterial entry. Experiments conducted with the laboratory strain E. coli K-12 EC901 carrying the recombinant plasmid pBJN406, which expresses Dr hemagglutinin, demonstrated that the dra operon is involved in polarized entry of IH11128 bacteria. Examined as a function of cell differentiation, the number of internalized bacteria decreased dramatically beyond cell confluency. Surviving intracellular IH11128 bacteria residing intracellularly had no

effect on the functional differentiation of Caco-2/TC7 cells.

L7 ANSWER 2 OF 25 MEDLINE
ACCESSION NUMBER: 2000134617 MEDLINE
DOCUMENT NUMBER: 20134617 PubMed ID: 10669375
TITLE: Vaccination with FimH **adhesin** protects cynomolgus monkeys from colonization and infection by uropathogenic Escherichia coli.
AUTHOR: Langermann S; Mollby R; Burlein J E; Palaszynski S R; Auguste C G; DeFusco A; Strouse R; Schenerman M A; Hultgren S J; Pinkner J S; Winberg J; Guldevall L; Soderhall M; Ishikawa K; Normark S; Koenig S
CORPORATE SOURCE: MedImmune, Inc., Gaithersburg, MD 20878, USA. langermanns@medimmune. com.
CONTRACT NUMBER: AI-29549 (NIAID)
DK-51406 (NIDDK)
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (2000 Feb) 181 (2) 774-8.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000413

AB Escherichia coli FimH **adhesin** mediates binding to the bladder mucosa. In mice, a FimH vaccine protects against bacterial challenge. In this study, 4 monkeys were inoculated with 100 microgram of FimCH **adhesin**-chaperone complex mixed with MF59 adjuvant, and 4 monkeys were given adjuvant only intramuscularly. After 2 doses (day 0 and week 4), a booster at 48 weeks elicited a strong IgG **antibody** response to FimH in the vaccinated monkeys. All 8 monkeys were challenged with 1 mL of 108 E. coli cystitis isolate NU14. Three of the 4 vaccinated monkeys were protected from bacteruria and pyuria; all control monkeys were infected. These findings suggest that a vaccine based on the FimH **adhesin** of E. coli type 1 pili may have utility in **preventing** cystitis in humans.

L7 ANSWER 3 OF 25 MEDLINE
ACCESSION NUMBER: 1998214883 MEDLINE
DOCUMENT NUMBER: 98214883 PubMed ID: 9554264
TITLE: Systemic immunization with conserved pilus-associated **adhesins** protects against mucosal infections.
AUTHOR: Palaszynski S; Pinkner J; Leath S; Barren P; Auguste C G; Burlein J; Hultgren S; Langermann S
CORPORATE SOURCE: Department of Mucosal Immunity and Vaccines, MedImmune, Inc., Gaithersburg, MD, USA.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1998) 92 117-22.
Journal code: 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806

ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB Colonization and infection of the bladder mucosa by Escherichia coli, the major uropathogenic organism, is dependent on the expression of pilus organelles. Type 1 pili are expressed by the majority of E. coli strains derived from patients with cystitis and pyelonephritis. FimH is the **adhesin** protein located at the distal tip of the heteropolymeric type-1 pilus which mediates binding to bladder cells through mannose receptors. We have shown that humoral **antibody** raised against two forms of purified FimH **adhesin** inhibited 94% (49/52) of E. coli **UTI** clinical isolates from binding to bladder tissue in vitro. Animals immunized with FimH-containing vaccines by a systemic route reduced colonization of the bladder mucosa in vivo in a murine cystitis model by > 99%. IgG **antibody** to FimH was detected in urinary samples obtained from immunized, protected mice. Passive systemic **administration** of immune sera from FimH-inoculated mice to naive animals also resulted in reduced colonization of bladder mucosa by uropathogenic E. coli. These studies demonstrate that systemic immunization with an anti-bacterial vaccine targeting a highly conserved **adhesin** on uropathogenic E. coli can induce IgG-mediated protection at a mucosal surface and may be a means of **preventing** recurrent and acute infections of the urogenital tract mucosa.

L7 ANSWER 4 OF 25 MEDLINE
ACCESSION NUMBER: 97426474 MEDLINE
DOCUMENT NUMBER: 97426474 PubMed ID: 9276729
TITLE: Localization of a domain in the FimH **adhesin** of Escherichia coli type 1 fimbriae capable of receptor recognition and use of a domain-specific **antibody** to confer protection against experimental **urinary tract infection**.
AUTHOR: Thankavel K; Madison B; Ikeda T; Malaviya R; Shah A H; Arumugam P M; Abraham S N
CORPORATE SOURCE: Department of Pathology, Barnes-Jewish Hospital, St. Louis, Missouri 63110, USA.
CONTRACT NUMBER: AI 35678 (NIAID)
DK 50814 (NIDDK)
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1997 Sep 1) 100 (5) 1123-36.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971008
Last Updated on STN: 20021026
Entered Medline: 19970925

AB The FimH subunit of type 1-fimbriated Escherichia coli has been implicated as an important determinant of bacterial adherence and colonization of the urinary tract. Here, we sought to localize the functionally important domain(s) within the FimH molecule and to determine if **antibodies** against this domain would block adherence of type 1-fimbriated E. coli to the bladder mucosa in situ

and in vivo in an established mouse model of cystitis. We generated translational fusion proteins of disparate regions of the FimH molecule with an affinity tag MalE, and tested each of the fusion products in vitro for functional activity. The minimum region responsible for binding mouse bladder epithelial cells and a soluble mannoprotein, horseradish peroxidase, was contained within residues 1-100 of the FimH molecule. We validated and extended these findings by demonstrating that **antibodies** directed at the putative binding region of FimH or at synthetic peptides corresponding to epitopes within the binding domain could specifically block type 1 fimbriae-mediated bacterial adherence to bladder epithelial cells in situ and yeast cells in vitro. Next, we compared the ability of mice passively immunized intraperitoneally with antisera raised against residues 1-25 and 253-264 of FimH or 1-13 of FimA to resist bladder colonization in vivo after intravesicular challenge with type 1-fimbriated E. coli. Only the **antibody** directed at the putative binding region of FimH (anti- s-FimH1-25) significantly reduced E. coli **bladder infections** in the experimental mouse model of **urinary tract infections**. Similar results were obtained when the mice were actively immunized with synthetic peptides corresponding to residues 1-25 and 253-264 of FimH or 1-13 of FimA. The mechanism of protection was attributed, at least in part, to inhibition of bacterial adherence to the bladder surface by s-FimH1-25-specific **antibody** molecules that had filtered through the kidneys into the urine. The level of FimH **antibodies** entering the bladder from the circulatory system of the immunized mice was found to be markedly enhanced upon bacterial challenge. The potential broad spectrum activity of the protective FimH **antibody** was indicated from its serologic cross-reactivity with various urinary tract bacterial isolates bearing type 1 fimbriae. These findings could be relevant in the design of an efficacious and broadly reactive FimH vaccine against **urinary tract infections**.

L7 ANSWER 5 OF 25 MEDLINE
ACCESSION NUMBER: 97284376 MEDLINE
DOCUMENT NUMBER: 97284376 PubMed ID: 9148412
TITLE: New vaccines may ward off **urinary tract infections**.
COMMENT: Comment on: Science. 1997 Apr 25;276(5312):607-11
AUTHOR: Service R F
SOURCE: SCIENCE, (1997 Apr 25) 276 (5312) 533.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19980206
Entered Medline: 19970509

L7 ANSWER 6 OF 25 MEDLINE
ACCESSION NUMBER: 93190449 MEDLINE
DOCUMENT NUMBER: 93190449 PubMed ID: 8447048
TITLE: [The role of bacterial adhesion in **urinary**

tract infections].
Die Rolle der Bakterienadharenz bei Harnwegsinfekten.

AUTHOR: Schaeffer A J
SOURCE: UROLOGE. AUSGABE A, (1993 Jan) 32 (1) 7-15. Ref: 53
Journal code: 1304110. ISSN: 0340-2592.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930416
Last Updated on STN: 19930416
Entered Medline: 19930406

AB Bacteria adhere to and colonize almost any surface. The mechanism by which bacteria interact with the mucosal surface appears to involve specific molecular ligands or **adhesins** on the surface of the bacteria that interlock with specific receptor molecules on the surface to be colonized. Material adhesion allows the microorganisms to resist being washed away by the fluids and secretions that bathe mucosal surfaces and is a necessary prerequisite to growth, colonization, and subsequent infection. Many examples of the role of bacterial adherence to tissues of the host have been reported in the literature. The classic study is that of Smith and Linggood, who demonstrated that toxin-producing enteropathogenic Escherichia coli, which cause diarrhoea in swine, adhere selectively to the mucosal surfaces of the small intestine. Adherence is mediated by hair-like pili projecting from the surface of the cells. Production of these pili is controlled by a specific plasmid, the loss of which renders the cells avirulent although they continue to produce toxin. In addition, **antibody** to the pilus antigen **prevents** adherence and protects piglets against challenge with the piliated organisms. Thus, the **adhesin** is an essential virulence factor in enteropathogenic E. coli infections in swine. Similar studies in a variety of diseases including enterotoxigenic E. coli infections in men and rheumatic fever support the concept that specific bacterial adherence to host tissues is an important characteristic of many pathogenic microorganisms.

L7 ANSWER 7 OF 25 MEDLINE
ACCESSION NUMBER: 92392616 MEDLINE
DOCUMENT NUMBER: 92392616 PubMed ID: 1355657
TITLE: Microbial interaction with animal cell surface carbohydrates.
AUTHOR: Karlsson K A; Angstrom J; Bergstrom J; Lanne B
CORPORATE SOURCE: Department of Medical Biochemistry, University of Gothenburg, Sweden.
SOURCE: APMIS. SUPPLEMENTUM, (1992) 27 71-83. Ref: 34
Journal code: 8812090. ISSN: 0903-465X.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19921023

Last Updated on STN: 19950206
Entered Medline: 19921014

AB Microbes have selected primarily carbohydrates for attachment to host animal cells. Recent studies have revealed essential characteristics in the recognition of receptor carbohydrates. Of importance is the property of recognizing also sequences placed inside an oligosaccharide chain, which differs from most animal **antibodies**. This is the basis for series of isoreceptors with the minimum receptor sequence in common but with separate neighbouring groups. There are families of microbial ligands that show different preferences for members within one series of isoreceptors, indicating only slight differences in the complementary binding sites of the proteins. Such differences may explain shifts in the selectivity of separate host tissues for infection. A second characteristic is the low affinity interaction often found where simple receptor-containing saccharides are unable to inhibit attachment. Technical possibilities are rapidly developing for the design of synthetic receptor analogues to be used in the **therapy** of clinical infections. This is urgently needed in cases where no rational **therapy** exists today.

L7 ANSWER 8 OF 25 MEDLINE
ACCESSION NUMBER: 90093480 MEDLINE
DOCUMENT NUMBER: 90093480 PubMed ID: 1967170
TITLE: The Dr hemagglutinin, afimbrial **adhesins** AFA-I and AFA-III, and F1845 fimbriae of uropathogenic and diarrhea-associated Escherichia coli belong to a family of hemagglutinins with Dr receptor recognition.
AUTHOR: Nowicki B; Labigne A; Moseley S; Hull R; Hull S; Moulds J
CORPORATE SOURCE: Department of Microbiology and Immunology, Baylor College of Medicine, Houston, Texas 77030.
CONTRACT NUMBER: AI18462 (NIAID)
AI21009 (NIAID)
AI23771 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1990 Jan) 58 (1) 279-81.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19950206
Entered Medline: 19900201

AB The receptor specificities of four Escherichia coli cloned hemagglutinins, AFA-I, AFA-III, F1845 fimbriae, and the Dr hemagglutinin were studied. Evidence is provided that all four hemagglutinins recognize as their receptor the Dr blood group antigen. However, results of experiments using enzyme-**treated** erythrocytes and monoclonal **antibodies** indicate that the four **adhesins** recognize different epitopes on the Dr antigen and thus constitute a family of Dr receptor-recognizing bacterial **adhesins**. Furthermore, the same results suggest that the Dr antigen itself may be divided into subcomponents on the basis of bacterial **adhesins**.

L7 ANSWER 9 OF 25 MEDLINE
ACCESSION NUMBER: 90004692 MEDLINE
DOCUMENT NUMBER: 90004692 PubMed ID: 2551609
TITLE: Glycoprotein oligosaccharides as recognition structures.
AUTHOR: Feizi T
CORPORATE SOURCE: MRC Clinical Research Centre, Harrow, Middlesex, UK.
SOURCE: CIBA FOUNDATION SYMPOSIUM, (1989) 145 62-74, discussion 74-9. Ref: 43
Journal code: 0356636. ISSN: 0300-5208.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198911
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19900328
Entered Medline: 19891102

AB A series of observations--the pronounced changes in the expression and distribution of oligosaccharide antigens during embryonic development, cell differentiation and oncogenesis, the prominence of these changing structures (oncodevelopmental antigens) on the receptor for epidermal growth factor, and the stimulation of receptor autophosphorylation following their perturbation with **antibodies**--has suggested that the oligosaccharides of growth factor receptors and complementary lectins may be intimately involved in molecular recognition events in growth and differentiation processes. For elucidating oligosaccharide recognition by diverse cellular and secreted proteins and microbial **adhesins**, a new technique has been developed which involves the overlay of immobilized oligosaccharide probes (neoglycolipids) derived from glycoproteins and other sources. New insights have been gained into carbohydrate recognition by several mammalian lectins, and a novel receptor system has been discovered in Escherichia coli isolated from patients with **urinary tract infections**. This new technique seems ideal for elucidating oligosaccharide recognition in diverse biological settings, and for 'quality control' of the sugar chains of recombinant glycoproteins engineered for the purpose of **administration** to man.

L7 ANSWER 10 OF 25 MEDLINE
ACCESSION NUMBER: 87136216 MEDLINE
DOCUMENT NUMBER: 87136216 PubMed ID: 3818102
TITLE: Mediation of Staphylococcus saprophyticus adherence to uroepithelial cells by lipoteichoic acid.
AUTHOR: Teti G; Chiofalo M S; Tomasello F; Fava C; Mastroeni P
SOURCE: INFECTION AND IMMUNITY, (1987 Mar) 55 (3) 839-42.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198704
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19900303

Entered Medline: 19870408

AB **Treatment** of uroepithelial cells with lipoteichoic acid from Staphylococcus saprophyticus resulted in a decrease in the adherence of this organism. Similar effects were observed when bacteria were pretreated with the lipoteichoic acid ligands albumin and anti-polyglycerophosphate monoclonal **antibodies**. Lipoteichoic acid might behave as an **adhesin** of S. saprophyticus.

L7 ANSWER 11 OF 25 MEDLINE
ACCESSION NUMBER: 85206292 MEDLINE
DOCUMENT NUMBER: 85206292 PubMed ID: 2860067
TITLE: Protection against Escherichia coli-induced **urinary tract infections** with hybridoma **antibodies** directed against type 1 fimbriae or complementary D-mannose receptors.
AUTHOR: Abraham S N; Babu J P; Giampapa C S; Hasty D L; Simpson W A; Beachey E H
CONTRACT NUMBER: AI-07238 (NIAID)
AI-10085 (NIAID)
AI-13550 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1985 Jun) 48 (3) 625-8. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198507
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850710

AB Hybridoma **antibodies** directed against quaternary structural epitopes of the type 1 fimbrial **adhesin** of Escherichia coli or against D-mannose, the sugar determinant in the complementary host cell receptor, **prevented** the attachment of mannose-sensitive E. coli to various eucaryotic cells. Passive intraperitoneal **administration** of the fimbria-specific or D-mannose-specific **antibodies** protected mice against retrograde colonization with mannose-sensitive E. coli instilled into their urinary bladders. Monoclonal **antibodies** directed against fimbrial subunits rather than quaternary structural epitopes or against N-acetylgalactosamine rather than D-mannose residues lacked protective activity. These studies provide evidence that bacterial colonization can be blocked or interrupted by **antibodies** directed against either the **adhesin** or the complementary host cell receptor of pathogenic microorganisms.

L7 ANSWER 12 OF 25 MEDLINE
ACCESSION NUMBER: 83081596 MEDLINE
DOCUMENT NUMBER: 83081596 PubMed ID: 6129198
TITLE: Recent progress in the understanding of the role of bacterial adhesion in the pathogenesis of **urinary tract infection.**
AUTHOR: Svanborg Eden C; Hagberg L; Leffler H; Lomberg H
SOURCE: INFECTION, (1982 Sep-Oct) 10 (5) 327-32. Ref: 24
Journal code: 0365307. ISSN: 0300-8126.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198302
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19950206
Entered Medline: 19830214

AB There is extensive evidence indicating that the capacity of Escherichia coli to attach to the mucosal lining of the urinary tract is a virulence factor in acute pyelonephritis in the unobstructed state. In vitro results using human uroepithelial cells and clinical E. coli isolates as well as in vivo work on ascending **urinary tract infection** in mice and E. coli strains with genetically defined **adhesins** support this notion. The biochemical characterization of the bacterial ligands and epithelial cell receptors important for the attachment of most pyelonephritogenic E. coli provides a more sophisticated means of evaluating the role of bacterial adhesion in **urinary tract infection**: 1) It allows precise diagnosis of the receptor specificity of clinical isolates; 2) The receptor can be used to isolate the relevant bacterial **adhesins**; 3) The localization and quantity of the receptor in the patient may be of prognostic importance; 4) The **administration** of soluble receptor analogues or **antibodies** to the **adhesins** may be useful for prophylactic and/or **therapeutic** purposes.

L7 ANSWER 13 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:570902 BIOSIS
DOCUMENT NUMBER: PREV200200570902
TITLE: Type-1 pili in the Gram-positive bacterial pathogen Enterococcus faecalis.
AUTHOR(S): Lyon, W. R. (1); Kau, A. L. (1); Hultgren, S. J. (1)
CORPORATE SOURCE: (1) Washington University, Saint Louis, MO USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 44. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 102nd General Meeting of the American Society for Microbiology Salt Lake City, UT, USA May 19-23, 2002 American Society for Microbiology . ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB **Urinary tract infections (UTIs**) are a common infection that affects a large proportion of the world's population, and account for significant morbidity and medical expenditures. While the primary cause of these infections are due to the Gram-negative bacterium Escherichia coli, a significant percentage of cases result from infections with the Gram-positive bacteria Enterococcus faecalis or Enterococcus faecium. Although it is known that colonization of the bladder by E. coli is facilitated by the type-1 pilus, that is encoded by the fire operon, nothing is known about the molecular basis of enterococcal disease. With the recent release of genome sequence from these two enterococcal species, we have identified the presence of numerous targets with potential to be required for the establishment of **UTIs**, including the fim operon. To determine whether these

structures are able to form, we performed an electron microscopy examination of the bacteria and were able to identify structures on the surface of the bacteria that resembled type-1 pili of E. coli. Western blot analysis was also able to confirm that these bacteria produce a protein which cross-reacts with anti-FimH (tip **adhesin**) **antibody**, and that the bacteria possess a binding activity similar to that contributed to E. coli by FimH. These results were confirmed to be due to the presence of the fim operon through a mutagenesis approach which **prevented** the pilus subunits from being expressed. The role of these structures in colonization was also confirmed through an in vivo mouse bladder colonization assay, which showed a large drop in colonization efficiency with the mutant E. faecalis compared to wild-type E. faecalis. These studies raise many questions not only regarding the exact mechanism that type-1 pili use in colonization, but also to their adaptation to accommodate Gram-positive bacterial architecture.

L7 ANSWER 14 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:231532 BIOSIS
DOCUMENT NUMBER: PREV199497244532
TITLE: Alanine-scanning mutagenesis reveals residues involved in binding of pap-3-encoded pili.
AUTHOR(S): Klann, Amy G.; Hull, Richard A.; Palzkill, Timothy; Hull, Sheila I. (1)
CORPORATE SOURCE: (1) Dep. Microbiol. Immunol., Baylor Coll. Med., One Baylor Plaza, Houston, TX 77030 USA
SOURCE: Journal of Bacteriology, (1994) Vol. 176, No. 8, pp. 2312-2317.
ISSN: 0021-9193.
DOCUMENT TYPE: Article
LANGUAGE: English
AB In order to identify functionally important residues in the pap-3-encoded **adhesin**, oligonucleotide-directed mutagenesis was used to substitute alanine(s) at sixteen positions in the **adhesin**. These alanine substitutions span nearly every domain and hydrophilic peak of the protein. The effects of these substitutions were measured by evaluating the patterns of hemagglutination exhibited by the mutant strains. It was found that strains harboring alanine substitutions at positions 88 and 89, 128 to 130, and 316 had lost the capacity to hemagglutinate. The presence of the mutated **adhesin** in the assembled pilus structure was verified by the reactions of purified pili with an **adhesin**-specific monoclonal **antibody** in an enzyme-linked immunosorbent assay and with a polyclonal **antibody** in Western blotting (immunoblotting). Alanine substitutions at positions 68, 110 and 111, and 143 to 146 had no effect upon hemagglutination, whereas substitutions at positions 203 and 204 and position 291 resulted in diminished binding. Thus, the residues necessary for hemagglutination are scattered throughout the **adhesin** in both the amino and carboxy regions. Delineation of these residues may prove useful in designing a **preventive treatment** that would cross-react with the essential binding residues from the **adhesins** of several different pyelonephritis-causing strains.

L7 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1984:339236 BIOSIS

DOCUMENT NUMBER: BA78:75716
TITLE: INHIBITION OF BACTERIAL ADHERENCE TO RAT BLADDER EPITHELIAL CELLS BY HUMAN IMMUNE SERUM GLOBULIN.
AUTHOR(S): FADER R C; HOUSTON C W; DAVIS C P
CORPORATE SOURCE: DEP. MICROBIOL., UNIV. TEX. MED. BRANCH, GALVESTON, TEX. 77550, USA.
SOURCE: CURR MICROBIOL, (1984) 10 (1), 29-34.
CODEN: CUMIDD. ISSN: 0343-8651.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB The ability of commercial human immune serum globulin (HISG) to inhibit the adherence of **urinary tract infection** isolates to rat bladder epithelial cells was investigated utilizing an in vitro adherence system. Significant decreases in adherence were noted when strains of Escherchia coli, Klebsiella pneumoniae, Proteus mirabilis and Enterobacter cloacae were tested against 5 HISG preparations. An enzyme-linked immunosorbent assay [ELISA] indicated that all 5 HISG preparations also contained **antibodies** against type-1 pili isolated from K. pneumoniae. The presence of **antibodies** directed against a bacterial **adhesin** and the effectiveness of HISG in inhibiting the attachment of a wide range of urinary pathogens to bladder cells suggest that HISG may have practical **therapeutic** values in the prophylaxis of diseases where bacterial adherence is a prerequisite for the initiation of infection.

L7 ANSWER 16 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97248188 EMBASE
DOCUMENT NUMBER: 1997248188
TITLE: [The importance of **urinary tract infection** for the development of renal insufficiency].
KANN EINE HARNWEGSINFEKTION ZUR NIERENINSUFFIZIENZ FUHREN?.
AUTHOR: Funfstuck R.; Stein G.
CORPORATE SOURCE: Dr. R. Funfstuck, Erlanger Allee 101, D-07740 Jena, Germany
SOURCE: Nieren- und Hochdruckkrankheiten, (1997) 26/6 (246-251).
Refs: 37
ISSN: 0300-5224 CODEN: NIHOD
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 028 Urology and Nephrology
LANGUAGE: German
SUMMARY LANGUAGE: English; German

AB Course and severity of **urinary tract infections** are determined by the efficacy of the host's defensive mechanisms on the one hand, and by the pathogenicity and virulence of the infective microorganism on the other. Uropathogenic microorganisms can develop a number of specific properties (0- and K-antigens, **adhesins**, hemolysins, serum resistance mechanisms, aerobactins etc.) enabling them to colonize the urogenital tract and to overcome the epithelial boundary layer of the urinary tract and the kidneys. Infection develops as a result of colonization, adhesion, internalization, and invasion. Due to an activation of the complement cascade, the release of cytokines,

growth factors, and adhesion molecules as well as of the recruitment of granulocytes, macrophages, and lymphocyte subpopulations, immunoregulatory processes may be initiated. Predisposing factors for the manifestation of an infection are deformities, and obstructions of the urinary tract (insufficiency of the urethral valve, disturbed micturition, strictures, compression, reflux, formation of urinary calculi), impairment of local defence mechanisms due to metabolic disorders (diabetes mellitus, hyperuricemia, nephrocalcinosis), or humoral and/or cellular immunodeficiency (disturbed local **antibody** production, sIgA deficiency), immunosuppressive **therapeutic** procedures, and existing disturbances of renal function. In general, **urinary tract infections** do not necessarily result in renal insufficiency. But, in case of a preexisting damage of the renal parenchyma, an infection may dramatically influence the course of the disease and the progress of renal insufficiency.

L7 ANSWER 17 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 83234590 EMBASE
DOCUMENT NUMBER: 1983234590
TITLE: [Medical aspects of **urinary tract infections**].
ASPECTS MEDICAUX DES INFECTIONS DE L'APPAREIL URINAIRE.
AUTHOR: Dupont B.; Fauchere J.L.
CORPORATE SOURCE: Hop. Inst. Pasteur, F 75015 Paris, France
SOURCE: Journal d'Urologie, (1983) 89/5 (299-307).
CODEN: JOURDD
COUNTRY: France
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
028 Urology and Nephrology
004 Microbiology
LANGUAGE: French
SUMMARY LANGUAGE: English

AB The authors undertake a general review of recent advances in the field of **urinary tract infections**.
Attention is drawn to the fact that bacteria can proliferate only if they adhere to the wall of the urinary tract before penetrating the epithelial cells. This adhesion is dependent upon **adhesins** which, in the urinary tract, can fix only upon specific receptors. It can therefore be understood that a mucosa bearing many receptors can easily be reinfected with organisms with the intestinal flora as their point of departure, via perineal and peri-urethral meatal infestation in the woman. A recent **therapeutic** advance is based upon the use of .beta.-lactamase inhibitors. A beta-lactamine neutralises the beta-lactamase produced by the organism and the other beta-lactamine acts as an antibiotic and kills the organism. This combination of two lactamines will probably be increasingly widely used in dealing with organisms. It is important to note that bacteriologists draw attention to the need to detect congenital abnormalities or foreign bodies or neighbouring infections, before incriminating only problems of bacterial virulence and the abnormally abundant presence of receptors on the urethrovesical mucosa. In the absence of urological disease, the **treatment** of lower **urinary tract infections** in the woman is not based upon any particular rules since short-term

treatment seems just as effective as long-term **treatment**. The problem is completely different in the **treatment** of acute pyelonephritis which requires a minimum of three weeks using an antibiotic with powerful tissue diffusion. The laboratory plays an important role in the diagnosis and **treatment** of such **urinary tract infections**. Study of bacteriuria, pyuria, detection of **antibodies** fixed to urinary bacteria, detection of serum **antibodies** specific for the bacterium, and the measurement of urinary levels of lacticodehydrogenase iso-enzyme 5 (LDH 5) currently form part of the investigations offered by bacteriology laboratories to those involved in the **treatment** of **urinary tract infections**.

L7 ANSWER 18 OF 25 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-528681 [56] WPIDS
DOC. NO. CPI: C2002-149653
TITLE: Novel peptide immunogen, useful for evoking **antibodies** to **prevent** adherence of Escherichia coli to bladder mucosa, comprises a FimH **adhesin** functional site-derived target peptide covalently linked to helper T cell epitope.
DERWENT CLASS: B04
INVENTOR(S): WANG, C Y
PATENT ASSIGNEE(S): (UNBI-N) UNITED BIOMEDICAL INC
COUNTRY COUNT: 99
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002051860	A2	20020704	(200256)*	EN	62

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002051860	A2	WO 2001-US50816	20011221

PRIORITY APPLN. INFO: US 2000-747802 20001222
AN 2002-528681 [56] WPIDS
AB WO 200251860 A UPAB: 20020903
NOVELTY - A peptide immunogen (I), comprising a helper T cell epitope sequence (Th) or a carrier protein covalently attached to a FimH **adhesin** functional site-derived (FAFSD) target peptide comprising not more than 30 amino acids of the carbohydrate binding pocket of FimH, or its crossreactive and immunologically functional analog or mimetope, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) FAFSD target peptide (II), comprising a sequence of FACKTANGTAIPIGGESANVYVNLA (S3), CDYPETITC (S6), CILRQTNNYNSDDFQFVL (S8) and its crossreactive and immunologically functional analog or mimetope;

(2) Synthetic peptide (III) of 20-100 amino acids, comprises an invasin domain, a helper T cell (Th) epitope, and a target peptide not more than 30 amino acids of the carbohydrate binding pocket of FimH, or its crossreactive and immunologically functional analog or mimetope;

(3) Pharmaceutical composition (IV), comprising (I) or (III) and a vaccine delivery vehicle; and

(4) Polymer (V) of at least two FAFSD peptide cross-linked by a bifunctional crosslinking agent.

ACTIVITY - Antibacterial.

No biological data available.

MECHANISM OF ACTION - Inhibitor of binding of type 1 fimbriated Escherichia coli to mouse bladder epithelial cell lines; Inhibitor of type 1 fimbriae-induced yeast cell aggregation.

FAFSD peptide specific antisera mediated inhibition of binding of type 1 fimbriated Escherichia coli to mouse bladder epithelial cell lines in vitro was assayed.

1 multiply 10-8 E.coli (50 mu l) were preincubated with an equal volume of various concentrations of **antibody** for 30 minutes at 37 deg. C. After which, this mixture was poured on a cover slip containing a monolayer of 1 multiply 105 bladder epithelial cells. The mixture was incubated for 1 hour after which the monolayer was vigorously washed to remove all loosely adherent bacteria. The monolayer was fixed and stained with methylene blue.

Inhibition of bacterial adherence was determined by microscopic counting of the number of adherent bacteria per 200 epithelial cells. Degree of inhibition was graded from + to 4+ for various immune sera in comparison to that of a panel of normal sera.

USE - (I) as (IV) are useful for inducing anti-FAFSD peptide **antibody** production in a mammal.

(IV) is also useful for reducing adherence to the urinary tract mucosa of a mammal by type 1 fimbriated uropathogenic enterobacteria (Escherichia coli) to **prevent urinary tract infection** (claimed).

(I) is useful for evoking **antibodies** for **preventing** adherence of E.coli and other enterobacteria to the bladder mucosa to confer protection against **urinary tract infection.**

ADVANTAGE - (I) has a focused FAFSD site-specific immunity together with a broad protective immunity, and with less adverse side reactions than the more complex polypeptide subunit vaccines and the carrier conjugated vaccine. Since (I) is chemically well defined it is easy and less costly to manufacture and to control or assure the quality of the product.

Dwg.0/1

L7 ANSWER 19 OF 25 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-280859 [32] WPIDS
DOC. NO. CPI: C2002-082628
TITLE: Stimulating immune response in a primate for **preventing, treating** bacterial induced diseases such as diseases of urinary tract, by **administering** bacterial adhesive proteins, preferably FimC-FimH polypeptide complex.

DERWENT CLASS: B04 D16
INVENTOR(S): BALLOU, W R; LANGERMANN, S
PATENT ASSIGNEE(S): (MEDI-N) MED IMMUNE INC; (MEDI-N) MEDIMMUNE INC
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002015928	A1	20020228	(200232)*	EN	92
AU 2001018049	A	20020304	(200247)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002015928	A1	WO 2000-US32398	20001128
AU 2001018049	A	AU 2001-18049	20001128

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001018049	A	Based on	WO 200215928

PRIORITY APPLN. INFO: US 2000-226146P 20000818
AN 2002-280859 [32] WPIDS
AB WO 200215928 A UPAB: 20020521
NOVELTY - Inducing in a primate immunoglobulin (Ig) molecules that bind a bacterial **adhesin** protein, preferably an attachment domain of a type 1 pilin polypeptide associated with a bacterium causing urogenital tract infections, comprising **administering** a purified peptide comprising antigenic fragment of type 1 **adhesin**, preferably attachment domain of type 1 pilin polypeptide to induce Ig molecules, is new.

DETAILED DESCRIPTION - Inducing (M) in a primate immunoglobulin (Ig) molecules that bind a bacterial **adhesin** protein, preferably an attachment domain of a type 1 pilin polypeptide associated with a bacterium causing urogenital tract infections, comprising inducing Ig molecules that bind a bacterial type 1 **adhesin**, particularly an attachment domain of a type 1 pilin polypeptide associated with a bacterium causing urogenital tract infections, or Ig molecules that inhibit binding of a bacterium causing urogenital tract infections to urogenital tract epithelial cells, by **administering** to a primate, a purified peptide (P) or peptide complex (PC) comprising an antigenic fragment of type 1 **adhesin**, preferably attachment domain of type 1 pilin polypeptide to induce Ig molecules in the urine or genital secretions of the primate, to reduce or **prevent** incidence of urogenital tract infections in the primate.

INDEPENDENT CLAIMS are also included for the following:
(1) vaccinating a primate against urogenital tract infection,

by **administering** to the primate, a purified nucleic acid containing a nucleotide sequence encoding (P) or PC to produce Ig molecules that specifically bind the type 1 pilin;

(2) a pharmaceutical composition comprising PC of an antigenic fragment of type 1 **adhesin**, in particular FimH and FimC protein, suitable for **administration** to humans;

(3) thermally or chemically stable pharmaceutical composition that is suitable for reconstitution into an injectable sterile and particulate-free solution, comprising a purified PC of a FimH and FimC protein;

(4) a sterile unit dosage form comprising 490 micro g/ml purified PC of a FimH and FimC protein; and

(5) a kit comprising a container comprising a composition comprising a purified PC of a FimH and FimC protein, and another container comprising a second composition comprising an adjuvant.

ACTIVITY - Antibacterial.

A FimCH composition comprising FimH and FimC molecules was tested in a randomized, controlled, double blind Phase I clinical trial in 48 healthy adult women. Four cohorts of 12 subjects were randomized at ratio of 3:1 and in a sequential fashion, given intramuscular doses of vaccine or control. FimCH was prepared for injection into a subject immediately prior to the injection. Doses of either 1, 5, 25 or 123 micro g of FimCH in 0.5 ml of squalene-based adjuvant (MF59C.1), or the control (MF59.C1 alone) were injected slowly, i.e. 20 to 30 seconds, into the deltoid muscle of the upper arm of the subjects at day 0, followed by a booster dose at 28 days followed by a second booster dose at 180 days. The vaccine was safe and well tolerated at all doses upon **administration** of the vaccination protocol. Mild to moderate pain at the site of injection was the most common adverse event. In addition, mild or moderate headaches, fatigue, and myalgias were observed and all adverse events resolved within 3-4 days. No serious adverse events were reported and no subject was discontinued due to adverse events. The FimCH vaccine was immunogenic in the human subjects and showed evidence of clear dose response. All vaccine recipients developed serum IgG **antibodies** to FimH by enzyme linked immunosorbent assay (ELISA) and western blot. Subjects with the best serum responses, i.e. highest levels of anti-FimH-T3 IgGs, also had IgG against FimH detected in urine and vaginal secretions after immunization and immune serum inhibited the binding of uropathogenic Escherichia coli to a J82 human uroepithelial cell line in vitro.

MECHANISM OF ACTION - Vaccine.

USE - (M) is useful for inducing IgG molecules in a primate, especially human to reduce or **prevent** the incidence of urogenital tract infection, in particular a **urinary tract infection, bladder infection** or kidney infection, caused by a bacterium of the family Enterobacteriaceae, preferably E. coli. The human has suffered more than two urogenital infections within one year, has asymptomatic bactourea, is a pregnant woman or a diabetic, is immonocompromised, has a human immonodeficiency virus (HIV) infection, has cancer, or is in remission from cancer, or is at risk for end stage renal disease. (M) is useful for vaccinating a primate against urogenital tract infection, for **treating** or ameliorating the symptoms of urogenital tract infection in a primate, and also slowing or **preventing** progression of a urinary track infection into end stage renal disease. (All claimed).

Dwg.0/4

L7 ANSWER 20 OF 25 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-171702 [22] WPIDS
DOC. NO. CPI: C2002-053139
TITLE: New immunogenic polypeptide, useful as vaccine for protecting against an **enterobacillus** -related **disease** in a patient at risk of contracting such disease, e.g. **urinary tract infection** or a **bladder infection.**
DERWENT CLASS: B04 D16
INVENTOR(S): AUGUSTE, C; BURLEIN, J; LANGERMANN, S; REVEL, A
PATENT ASSIGNEE(S): (MEDI-N) MED IMMUNE INC; (AUGU-I) AUGUSTE C; (BURL-I) BURLEIN J; (LANG-I) LANGERMANN S; (REVE-I) REVEL A; (MEDI-N) MEDIMMUNE INC
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002004496	A2	20020117	(200222)*	EN	101
AU 2001071907	A	20020121	(200234)		
US 2002150587	A1	20021017	(200270)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002004496	A2	WO 2001-US21525	20010706
AU 2001071907	A	AU 2001-71907	20010706
US 2002150587	A1 Provisional	US 2000-216750P	20000707
		US 2001-900575	20010706

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001071907	A Based on	WO 200204496

PRIORITY APPLN. INFO: US 2000-216750P 20000707; US 2001-900575 20010706
AN 2002-171702 [22] WPIDS
AB WO 200204496 A UPAB: 20020409
NOVELTY - An immunogenic polypeptide, which comprises residues 26 to 186 of any of 24 279 or 280 residue amino acid sequences (S1), all fully defined in the specification, is new. It includes a consensus sequence of FimH proteins.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated polynucleotide encoding the novel polypeptide;

(2) a vaccine composition comprising the immunogenic polypeptide, in a carrier;

(3) an **antibody** that binds to a polypeptide having (S1);

(4) a process for protecting against an **enterobacillus** -related **disease** in a patient at risk of contracting such disease by **administering** the vaccine composition;

(5) processes for **treating** an **enterobacillus** -related **disease** in a patient afflicted with the disease by **administering** the vaccine composition or the **antibody**;

(6) a recombinant cell expressing the novel polypeptide;

(7) a vector comprising a polynucleotide encoding the novel polypeptide; and

(8) a process for producing the novel polypeptide comprising expressing the polypeptide from a recombinant cell containing the vector of (7).

ACTIVITY - Antibacterial.

No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The vaccine composition or the **antibody** is useful for protecting against an **enterobacillus**-related **disease** in a patient at risk of contracting the disease. The vaccine or **antibody** is also useful for **treating** an **enterobacillus**-related **disease** in a patient afflicted with it. In particular, the disease is a urinary tract or **bladder infection**. The disease is caused by a bacterium of the family Enterobacteriaceae, particularly Escherichia coli. (All claimed).

Dwg.0/6

L7 ANSWER 21 OF 25 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-082937 [11] WPIDS

DOC. NO. CPI: C2002-025091

TITLE: Immunizing composition, useful for stimulating production of **antibodies** in the **treatment** of **urinary tract infection** vaccine, comprises anti-idiotypic **antibody** or antigen-binding fragment.

DERWENT CLASS: B04 D16

INVENTOR(S): WU, X

PATENT ASSIGNEE(S): (WUXX-I) WU X; (UYNY) UNIV NEW YORK STATE

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001087233	A2	20011122	(200211)*	EN	44

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

US 2002028200 A1 20020307 (200221)

AU 2001061371 A 20011126 (200222)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001087233 A2		WO 2001-US15095	20010510
US 2002028200 A1	Provisional	US 2000-204572P	20000516
		US 2001-852283	20010510
AU 2001061371 A		AU 2001-61371	20010510

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001061371 A		Based on	WO 200187233

PRIORITY APPLN. INFO: US 2000-204572P 20000516; US 2001-852283 20010510

AN 2002-082937 [11] WPIDS

AB WO 200187233 A UPAB: 20020215

NOVELTY - An immunizing composition comprising an anti-idiotypic **antibody** or antigen-binding fragment which binds to an idiotype of a second **antibody** which binds an epitope of FimH **adhesin** from uropathogenic Type I-fimbriated Escherichia coli but not to FimH of non-uropathogenic type, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a hybridoma cell producing the anti-idiotypic **antibody**.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - FimH **adhesin** binder; vaccine. No supporting data is given.

USE - As an immunizing composition for stimulating and enhancing the production of **antibodies** (claimed) useful for **treatment** of **urinary tract infection** (**UTI**). It is also useful in immunoassays e.g. radio-, enzyme, chemiluminescence, fluorescence, immunoprecipitiation, latex agglutination, hemagglutionation immunoassays. Can also be used for qualitative and quantitative determination of **antibodies** directed against FimH from uropathogenic antigens.

ADVANTAGE - The **antibodies** mimic the antigenic determinants of FimH **adhesin**. Unlimited amounts of vaccine (**antibodies**) can be produced having highly immunogenic molecules. The **antibody** recognize and bind to FimH **adhesin** of uropathogenic Type I-fimbriated Escherichia coli but not to FimH of non-uropathogenic Type I-fimbriated E. coli thus averting potentially serious side effects caused by the elimination of beneficial intestinal E. coli flora.

Dwg.0/0

L7 ANSWER 22 OF 25 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-159539 [16] WPIDS

DOC. NO. CPI: C2001-047460

TITLE: Polypeptides useful as vaccines for **prevention** and/or **treatment** of diseases such as **urinary tract infections**, caused by Enterobacteriaceae, comprises mannose-binding domains derived from **adhesin** molecules.

DERWENT CLASS: B04 D16
INVENTOR(S): HULTGREN, S J; LANGERMANN, S
PATENT ASSIGNEE(S): (MEDI-N) MED IMMUNE INC; (MEDI-N) MEDIMMUNE INC
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001005978	A1	20010125	(200116)*	EN	53

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000063497	A	20010205	(200128)	
EP 1194563	A1	20020410	(200232)	EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001005978	A1	WO 2000-US19402	20000714
AU 2000063497	A	AU 2000-63497	20000714
EP 1194563	A1	EP 2000-950385	20000714
		WO 2000-US19402	20000714

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000063497	A	Based on	WO 200105978
EP 1194563	A1	Based on	WO 200105978

PRIORITY APPLN. INFO: US 1999-144016P 19990715
AN 2001-159539 [16] WPIDS
AB WO 200105978 A UPAB: 20010323
NOVELTY - A purified polypeptide (I) comprising one or more domains, so that where more than one domain is present the domains are attached to each other by chemical linking structures of a length less than 25 amino acids, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an immunogenic composition (II) comprising a purified polypeptide comprising a portion of **adhesin** protein FimH, selected from mannose binding-domains MBD-1, MBD-2, MBD-3, COL and MBD-C (the polypeptide is other than FimH or a polypeptide comprising FimH);

(2) a polynucleotide comprising a coding region for (I);

(3) an **antibody** (III) specific for (I);

(4) a composition comprising (I) or (III); and

(5) a vaccine (IV) comprising (I) or (II).

ACTIVITY - Antibacterial.
No supporting data is given.
MECHANISM OF ACTION - Vaccine.
USE - (IV) is useful for **prevention** and/or

treatment of diseases, such as **urinary tract infection** caused by a bacterium of the family Enterobacteriaceae, especially Escherichia coli in animals, in particular humans (claimed). (I) is useful as an immunogen to stimulate the production of **antibodies** for use in passive immunotherapy, as diagnostic reagent and as reagents in other processes such as affinity chromatography. The **antibodies** are useful for research purposes for studying protein-lectin or collagen binding and interactions. (II) is useful for producing **antibodies** to diagnose **urinary tract infections**, to produce vaccines for prophylaxis and/or **treatment** of such infection as well as booster vaccines to maintain a high titer of **antibodies** against the immunogen(s) of (II).
Dwg.0/5

L7 ANSWER 23 OF 25 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-256496 [22] WPIDS
DOC. NO. CPI: C2000-078210
TITLE: Immunizing patients to **treat** staphylococcal infections comprises **administering** immunoglobulins having higher **antibody** titer to staphylococcal **adhesin** protein.
DERWENT CLASS: B04 D16
INVENTOR(S): FOSTER, T J; HOOK, M; PATTI, J M
PATENT ASSIGNEE(S): (INHI-N) INHIBITEX INC; (QUEE-N) QUEEN ELIZABETH COLLEGE DUBLIN; (TEXA) UNIV TEXAS A & M SYSTEM; (FOST-I) FOSTER T J; (HOOK-I) HOOK M; (PATT-I) PATTI J M
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000012132	A1	20000309	(200022)*	EN	84
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 9956966	A	20000321	(200031)		
NO 2001000981	A	20010426	(200131)		
EP 1121149	A1	20010808	(200146)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002523474	W	20020730	(200264)		88
US 2002159997	A1	20021031	(200274)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000012132	A1	WO 1999-US19729	19990831
AU 9956966	A	AU 1999-56966	19990831
NO 2001000981	A	WO 1999-US19729	19990831
		NO 2001-981	20010227

Searcher : Shears 308-4994

EP 1121149	A1		EP 1999-943981	19990831
			WO 1999-US19729	19990831
JP 2002523474	W		WO 1999-US19729	19990831
			JP 2000-567243	19990831
US 2002159997	A1	Provisional	US 1998-98449P	19980831
		Div ex	US 1999-386960	19990831
			US 2002-91494	20020307

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9956966	A	Based on	WO 200012132
EP 1121149	A1	Based on	WO 200012132
JP 2002523474	W	Based on	WO 200012132

PRIORITY APPLN. INFO: US 1998-98449P 19980831; US 1999-386960 19990831; US 2002-91494 20020307

AN 2000-256496 [22] WPIDS

AB WO 200012132 A UPAB: 20021105

NOVELTY - Immunizing patients to **treat** or **prevent** staphylococcal infection comprises **administering** immunologically effective amount of purified immunoglobulins (IG) obtained by **treating** donor plasma (I) having higher **antibody** (Ab) titer to staphylococcal **adhesin.**

DETAILED DESCRIPTION - Immunizing patients to **treat** or **prevent** staphylococcal infections comprising:

(a) providing a source of donor plasma having a higher than normal **antibody** titer to a staphylococcal **adhesin** ;

(b) **treating** the donor plasma to obtain purified immunoglobulin; and

(c) **administering** to the patient an immunologically effective amount of purified immunoglobulin-containing donor plasma.

INDEPENDENT CLAIMS are also included for the following:

(1) method of obtaining (I) comprises recovering plasma from the blood sample having higher Ab titer to staphylococcal **adhesin** and **treating** the donor plasma to obtain IG in a purified state that has higher Ab titer to staphylococcal **adhesin;**

(2) a donor plasma composition obtained by the method (2); and

(3) a kit (II) for identification of blood or plasma having higher titers of Ab comprises an antigen to a staphylococcal Ab, a support to bind the antigen and a detectable label that can be attached to the Ab.

ACTIVITY - Antibacterial; vulnerary. The effect of SA-IVIG MS502 (S) in the **treatment** of staphylococcal infection was tested using mice 5-6 weeks old. The animals were injected with 5.6 multiply 107 CFU Staphylococcus aureus (SA) 601 via the tail vein. The next day the animals were **treated** with single 0.5 ml intraperitoneal injection of (S). Control mice were left untreated. The mice were followed up for 5 days and were then sacrificed. The results showed that 93% of the mice that received (S) prior to SA challenge survived whereas only 76 % of the control mice survived the bacterial challenge, clearly indicating that the **administration** of ClfA donor selected human SA-IVIG provided a significant and effective **treatment** of staphylococcal infections.

MECHANISM OF ACTION - Vaccine.
USE - The method is useful for **treating** staphylococcal infections (claimed) and thereby **treats** mastitis, arthritis, endocarditis, septicemia, osteomyelitis, furunculosis, cellulitis, pyemia, pneumonia, pyoderma, suppuration of wounds, food poisoning and **bladder infections** . (II) is useful for identifying blood or plasma having higher **antibody** titers to staphylococcal **adhesin** (claimed).
ADVANTAGE - The method is useful for **treating** wide variety of staphylococcal infections.
Dwg.0/2

L7 ANSWER 24 OF 25 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1995-270467 [36] WPIDS
DOC. NO. CPI: C1995-122531
TITLE: New fimbriae **adhesins** from Escherichia coli strains CECT 4484 and 4485 - used to **treat** and **prevent urinary tract infections** by E. coli and to produce diagnostic **antibodies**.
DERWENT CLASS: B04 D16
INVENTOR(S): GARATE, A M; PELAEZ, R P; QUESADA, J M; BARANDIARAN, J M; MARTINEZ, GARATE A; MARTINEZ, QUESADA J; PALACIOS, PELAEZ R; PALACIOS, P R
PATENT ASSIGNEE(S): (INFA-N) IND FARM Y ESPECIALIDADES SA
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 666271	A1	19950809	(199536)*	EN	20
R: AT BE CH DE DK FR GB GR IE IT LI NL PT SE					
AU 9511503	A	19950817	(199541)		
CA 2141475	A	19950805	(199543)		
ES 2076895	A1	19951101	(199550)		
JP 08034798	A	19960206	(199615)		15
ES 2076895	B1	19960816	(199639)		
BR 9500546	A	19970527	(199727)		
AU 691221	B	19980514	(199831)		
JP 2851556	B2	19990127	(199909)		15
EP 666271	B1	19991020	(199948)	EN	
R: AT BE CH DE DK FR GB GR IE IT LI NL PT SE					
CA 2141475	C	19990824	(200001)	EN	
DE 69512808	E	19991125	(200002)		
MX 197377	B	20000705	(200160)		
US 6471966	B1	20021029	(200274)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 666271	A1	EP 1995-200257	19950202
AU 9511503	A	AU 1995-11503	19950201
CA 2141475	A	CA 1995-2141475	19950131
ES 2076895	A1	ES 1994-202	19940204
JP 08034798	A	JP 1995-16819	19950203
ES 2076895	B1	ES 1994-202	19940204

Searcher : Shears 308-4994

BR 9500546	A	BR 1995-546	19950206
AU 691221	B	AU 1995-11503	19950201
JP 2851556	B2	JP 1995-16819	19950203
EP 666271	B1	EP 1995-200257	19950202
CA 2141475	C	CA 1995-2141475	19950131
DE 69512808	E	DE 1995-612808	19950202
		EP 1995-200257	19950202
MX 197377	B	MX 1995-789	19950202
US 6471966	B1 Cont of CIP of	US 1995-383765	19950203
		US 1997-858903	19970519
		US 1998-128484	19980804

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 691221	B	Previous Publ.	AU 9511503
JP 2851556	B2	Previous Publ.	JP 08034798
DE 69512808	E	Based on	EP 666271

PRIORITY APPLN. INFO: ES 1994-202 19940204
AN 1995-270467 [36] WPIDS
AB EP 666271 A UPAB: 19950918
New type 1 and type P fimbriae **adhesins** (A) from the novel E. coli strains CECT 4484 and 4485 have mol. wt. 0.2-20 million, and comprise 90-95 wt.% protein and 1-3 wt.% sugar. Type 1 (A) has 5 protein fractions of mol. wt. 14-20 kDa, mainly (55%) a 17-18 kDa component associated with carbohydrates. The type P (A) has 5 protein fractions of mol. wt. 14-20 kDa, mainly 19-20 kDa (35%) and 15 kDa (30%) components, the first of which is associated with carbohydrate. The carbohydrate comprises alpha (1-3, 1-6 or 1-2) mannose-mannose units; alpha-sialic acid; alpha (2-6 or 2-3) galactose; galactose (1-3) N-acetylgalactosamine and galactose beta(1-4) N-acetylglucosamine.

USE - (A) are used to **treat** or **prevent** (as vaccines) **urinary tract infections** caused by fimbriated E. coli. The two types of (A) may be used together (there is almost no cross-reactivity between them). They can also be used to raise anti- (A) **antibodies**, useful for diagnosing and typing uropathogenic E. coli. (A) are **administered** (opt. with usual adjuvants) at 0.1-100 mug/kg, in 1-4 doses, usually by subcutaneous or intraperitoneal injection, but oral **admin**. is also contemplated.

ADVANTAGE - (A) can be produced in pure form, free of flagella, haemolysin and lipopolysaccharide (LPS).
Dwg.0/4

L7 ANSWER 25 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:467807 SCISEARCH
THE GENUINE ARTICLE: 205NN
TITLE: **Adhesins** as targets for vaccine development
AUTHOR: Wizemann T M; Adamou J E; Langermann S (Reprint)
CORPORATE SOURCE: MEDIMMUNE INC, DEPT IMMUNOL & MOL GENET, 35 W WATKINS MILL RD, GAITHERSBURG, MD 20878 (Reprint); MEDIMMUNE INC, DEPT IMMUNOL & MOL GENET, GAITHERSBURG, MD 20878
COUNTRY OF AUTHOR: USA

SOURCE: EMERGING INFECTIOUS DISEASES, (MAY-JUN 1999) Vol. 5, No. 3, pp. 395-403.
Publisher: CENTER DISEASE CONTROL, ATLANTA, GA 30333.
ISSN: 1080-6040.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 66

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Blocking the primary stages of infection, namely bacterial attachment to host cell receptors and colonization of the mucosal surface, may be the most effective strategy to **prevent** bacterial infections. Bacterial attachment usually involves an interaction between a bacterial surface protein called an **adhesin** and the host cell receptor. Recent preclinical vaccine studies with the FimH **adhesin** (derived from uropathogenic Escherichia coli) have confirmed that **antibodies** elicited against an **adhesin** can impede colonization, block infection, and **prevent** disease. The studies indicate that prophylactic vaccination with **adhesins** can block bacterial infections. With recent advances in the identification, characterization, and isolation of other **adhesins**, similar approaches are being explored to **prevent** infections, from otitis media and dental caries to pneumonia and sepsis.

FILE 'HCAPLUS' ENTERED AT 15:33:27 ON 03 DEC 2002
L8 0 S PCGA139? OR PCGA 139

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:34:31 ON 03 DEC 2002
L9 0 S L8

(FILE 'MEDLINE' ENTERED AT 15:34:52 ON 03 DEC 2002)

L10	1005	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"ADHESINS, BACTERIAL"/CT
L11	21416	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"URINARY TRACT INFECTIONS"/CT
L12	5712	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"BLADDER DISEASES"/CT
L13	3881	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"ENTEROBACTERIACEAE INFECTIONS"/CT
L14	36	SEA	FILE=MEDLINE	ABB=ON PLU=ON	L10 AND (L11 OR L12 OR L13)
L15	58737	SEA	FILE=MEDLINE	ABB=ON PLU=ON	ANTIBODIES/CT
L16	0	SEA	FILE=MEDLINE	ABB=ON PLU=ON	L14 AND L15

L10	1005	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"ADHESINS, BACTERIAL"/CT
L11	21416	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"URINARY TRACT INFECTIONS"/CT
L12	5712	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"BLADDER DISEASES"/CT
L13	3881	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"ENTEROBACTERIACEAE INFECTIONS"/CT
L14	36	SEA	FILE=MEDLINE	ABB=ON PLU=ON	L10 AND (L11 OR L12 OR L13)

L17	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	L14 AND (THERAPY OR THERAPEUTIC USE)/CT
L10	1005	SEA FILE=MEDLINE ABB=ON	PLU=ON	"ADHESINS, BACTERIAL"/CT
L11	21416	SEA FILE=MEDLINE ABB=ON	PLU=ON	"URINARY TRACT INFECTION S"/CT
L12	5712	SEA FILE=MEDLINE ABB=ON	PLU=ON	"BLADDER DISEASES"/CT
L13	3881	SEA FILE=MEDLINE ABB=ON	PLU=ON	"ENTEROBACTERIACEAE INFECTIONS"/CT
L14	36	SEA FILE=MEDLINE ABB=ON	PLU=ON	L10 AND (L11 OR L12 OR L13)
L18	3	SEA FILE=MEDLINE ABB=ON	PLU=ON	L14 AND ADMINISTRATION & DOSAGE/CT

L19 4 L17 OR L18

L19 ANSWER 1 OF 4 MEDLINE
AN 2001184845 MEDLINE
TI Vaccination utilizing the FimCH complex as a strategy to prevent Escherichia coli urinary tract infections.
AU Langermann S; Ballou W R Jr
SO JOURNAL OF INFECTIOUS DISEASES, (2001 Mar 1) 183 Suppl 1 S84-6.
Ref: 13
Journal code: 0413675. ISSN: 0022-1899.

L19 ANSWER 2 OF 4 MEDLINE
AN 2000134617 MEDLINE
TI Vaccination with FimH adhesin protects cynomolgus monkeys from colonization and infection by uropathogenic Escherichia coli.
AU Langermann S; Mollby R; Burlein J E; Palaszynski S R; Auguste C G; DeFusco A; Strouse R; Schenerman M A; Hultgren S J; Pinkner J S; Winberg J; Guldevall L; Soderhall M; Ishikawa K; Normark S; Koenig S
SO JOURNAL OF INFECTIOUS DISEASES, (2000 Feb) 181 (2) 774-8.
Journal code: 0413675. ISSN: 0022-1899.
AB Escherichia coli FimH adhesin mediates binding to the bladder mucosa. In mice, a FimH vaccine protects against bacterial challenge. In this study, 4 monkeys were inoculated with 100 microgram of FimCH adhesin-chaperone complex mixed with MF59 adjuvant, and 4 monkeys were given adjuvant only intramuscularly. After 2 doses (day 0 and week 4), a booster at 48 weeks elicited a strong IgG antibody response to FimH in the vaccinated monkeys. All 8 monkeys were challenged with 1 mL of 108 E. coli cystitis isolate NU14. Three of the 4 vaccinated monkeys were protected from bacteruria and pyuria; all control monkeys were infected. These findings suggest that a vaccine based on the FimH adhesin of E. coli type 1 pili may have utility in preventing cystitis in humans.

L19 ANSWER 3 OF 4 MEDLINE
AN 97284376 MEDLINE
TI New vaccines may ward off urinary tract infections.
AU Service R F
SO SCIENCE, (1997 Apr 25) 276 (5312) 533.
Journal code: 0404511. ISSN: 0036-8075.

L19 ANSWER 4 OF 4 MEDLINE
AN 97206960 MEDLINE
TI Progress on study of urinary tract infections.
AU Matsumoto T
SO FUKUOKA IGAKU ZASSHI. FUKUOKA ACTA MEDICA, (1996 Dec) 87 (12) 260-5.
Ref: 7
Journal code: 9423321. ISSN: 0016-254X.

FILE 'HCAPLUS' ENTERED AT 15:39:41 ON 03 DEC 2002
L20 60 SEA FILE=HCAPLUS ABB=ON PLU=ON (ENTEROBACTER? OR ENTERO BACTER?)(W)INFECT?
L21 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND ADHESIN

L22 2 L21 NOT L2

L22 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:518252 HCAPLUS
DOCUMENT NUMBER: 131:153726
TITLE: Inhibition of bacterial binding by high-mannose oligosaccharides, and method for the treatment of Gram-negative bacterial infections
INVENTOR(S): Smith, Sam; Elbein, Alan D.; Pan, Y. T.
PATENT ASSIGNEE(S): The Board of Trustees of the University of Arkansas, USA
SOURCE: U.S., 20 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5939279	A	19990817	US 1997-932876	19970918

AB A method is provided for the treatment of Gram-neg. bacterial infections using high-mannose contg. oligosaccharides. Specifically, the invention describes the use of Man9 (GlcNAc)2-hydrophobic glycopeptides (i.e. tyrosinamide) to block adhesion of the bacteria pili to the oligosaccharide of the host cells plasma membrane in infections of Enterobacter cloacae and other Enterobacter and gram-neg. species.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:507813 HCAPLUS
DOCUMENT NUMBER: 131:256057
TITLE: The mast cell tumor necrosis factor .alpha. response to FimH-expressing Escherichia coli is mediated by the glycosylphosphatidylinositol-anchored molecule CD48
AUTHOR(S): Malaviya, Ravi; Gao, Zhimin; Thankavel, Krishnan; Van der Merwe, P. Anton; Abraham, Soman N.
CORPORATE SOURCE: Department of Pathology and Microbiology, Duke

University Medical Center, Durham, NC, 27710, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(14), 8110-8115
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mast cells are well known for their harmful role in IgE-mediated hypersensitivity reactions, but their physiol. role remains a mystery. Several recent studies have reported that mast cells play a crit. role in innate immunity in mice by releasing tumor necrosis factor .alpha. (TNF-.alpha.) to recruit neutrophils to sites of **enterobacterial infection**. In some cases, the mast cell TNF-.alpha. response was triggered when these cells directly bound FimH on the surface of Escherichia coli. The authors have identified CD48, a glycosylphosphatidylinositol-anchored mol., to be the complementary FimH-binding moiety in rodent mast cell membrane fractions. The authors showed that (i) pretreatment of mast cell membranes with antibodies to CD48 or phospholipase C inhibited binding of FimH+ E. coli, (ii) FimH+ E. coli but not a FimH- deriv. bound isolated CD48 in a mannose-inhibitable manner, (iii) binding of FimH+ bacteria to Chinese hamster ovary (CHO) cells was markedly increased when these cells were transfected with CD48 cDNA, and (iv) antibodies to CD48 specifically blocked the mast cell TNF-.alpha. response to FimH+ E. coli. Thus, CD48 is a functionally relevant microbial receptor on mast cells that plays a role in triggering inflammation.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE' BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:45:15 ON 03 DEC 2002)

L23 27 S L21
L24 27 DUP REM L23 (0 DUPLICATES REMOVED)
L25 3 S L24 AND (THERAP? OR TREAT? OR PREVENT?)
L26 3 S L25 NOT L7

L26 ANSWER 1 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002374354 EMBASE
TITLE: Role of type 1 fimbria- and P fimbria-specific adherence in colonization of the neurogenic human bladder by Escherichia coli.
AUTHOR: Hull R.A.; Donovan W.H.; Del Terzo M.; Stewart C.; Rogers M.; Darouiche R.O.
CORPORATE SOURCE: R.A. Hull, Department of Molecular Virology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, United States. rhull@bcm.tmc.edu
SOURCE: Infection and Immunity, (2002) 70/11 (6481-6484).
Refs: 17
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
028 Urology and Nephrology
LANGUAGE: English

Searcher : Shears 308-4994

SUMMARY LANGUAGE: English

AB Recent clinical studies suggest that the deliberate colonization of the human bladder with a prototypic asymptomatic bacteriuria-associated bacterium, Escherichia coli 83972, may reduce the frequency of urinary tract infection in individuals with spinal cord injuries. However, the mechanism by which E. coli 83972 colonizes the bladder is unknown. We examined the role in bladder colonization of the E. coli 83972 genes papG and fimH, which respectively encode P and type 1 receptor-specific fimbrial **adhesins**. E. coli 83972 and isogenic papG.DELTA. and papG.DELTA. fimH.DELTA. mutants of E. coli 83972 were compared for their capacities to colonize the neurogenic human bladder. Both strains were capable of stable colonization of the bladder. The results indicated that type 1 class-specific adherence and P class-specific adherence, while implicated as significant colonization factors in experiments that employed various animal model systems, were not required for colonization of the neurogenic bladder in human beings. The implications of these results with regard to the selection of potential vaccine antigens for the **prevention** of urinary tract infection are discussed.

L26 ANSWER 2 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002049267 EMBASE
TITLE: Protection of suckling neonatal pigs against infection with an enterotoxigenic Escherichia coli expressing 987P fimbriae by the administration of a bacterial competitive exclusion culture.
AUTHOR: Genovese K.J.; Harvey R.B.; Anderson R.C.; Nisbet D.J.
CORPORATE SOURCE: K.J. Genovese, USDA-ARS-SPARC, 2881 F and B Road, College Station, TX 77845, United States. genovese@ffsru.tamu.edu
SOURCE: Microbial Ecology in Health and Disease, (2001) 13/4 (223-228).
Refs: 25
ISSN: 0891-060X CODEN: MEHDE6
COUNTRY: Norway
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
046 Environmental Health and Pollution Control
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The objective of these experiments was to evaluate the effects of a porcine-derived CE culture, RPCF, on an enterotoxigenic Escherichia coli infection in suckling neonatal pigs. Litters of piglets from 18 crossbred sows were included in the study. All piglets remained on-sow for the duration of these studies. Piglets in RPCF groups were orally administered 5 ml of the RPCF bacterial competitive exclusion culture within 12 h of birth. Control piglets were given sterile medium orally as a placebo within 12 h of birth. At 48 h of age, piglets in all groups were orally challenged with an enterotoxigenic E. coli expressing the 987P fimbrial **adhesin**. Daily rectal swabs were taken, mortalities were recorded, and at 5 days post-challenge, piglets in all groups were euthanized and necropsied. Samples were taken from the ileum, jejunum, ileocecal junction, cecum, colon, and ileocecal lymph nodes and cultured for the presence and enumeration of E. coli. Significant reductions ($p < 0.001$) were observed in all samples taken at necropsy from RPCF-

treated pigs when compared with control pigs. Both ileal and cecal concentrations of E. coli were reduced by 5 log(10) in those pigs that were administered the RPCF culture. A significant reduction in mortality was observed, decreasing from 23% in the control group to 2.7% in the RPCF group ($p < 0.001$). Clinical colibacillosis is a major economic and animal health concern in the swine industry. The RPCF CE culture may represent a means of possibly reducing the losses and morbidity associated with colibacillosis in pigs and, thus, may help to reduce the economic and animal health strains placed on the swine industry and the animals therein.

L26 ANSWER 3 OF 3 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999021809 EMBASE
TITLE: Oral, inactivated, whole cell enterotoxigenic Escherichia coli plus cholera toxin B subunit vaccine: Results of the initial evaluation in children.
AUTHOR: Savarino S.J.; Hall E.R.; Bassily S.; Brown F.M.; Youssef F.; Wierzba T.F.; Peruski L.; El-Masry N.A.; Safwat M.; Rao M.; El Mohamady H.; Abu-Elyazeed R.; Naficy A.; Svennerholm A.-M.; Jertborn M.; Lee Y.J.; Clemens J.D.
CORPORATE SOURCE: Dr. S.J. Savarino, c/o Research Publications Office, US Naval Medical Research Unit No. 3, Box 5000, FPO, AE 09835-0007, United States. savarino@namru.navy.mil
SOURCE: Journal of Infectious Diseases, (1999) 179/1 (107-114).
Refs: 38
ISSN: 0022-1899 CODEN: JIDIAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Two randomized, double-blinded trials assessed the safety and immunogenicity of an oral, killed enterotoxigenic Escherichia coli (ETEC) plus cholera toxin B subunit vaccine in Egyptian children. Two doses of vaccine or E. coli K-12 were given 2 weeks apart to 105 6- to 12-year-olds and 97 2- to 5-year-olds. Safety was monitored for 3 days after each dose. Blood was collected before immunization and 7 days after each dose to measure immune responses. Few children reported postdosing symptoms, with no differences in the frequency of symptoms between **treatment** groups. Most vaccinees had an IgA antibody-secreting cell response against colonization factor antigen I (100%, 6-12 years; 95%, 2-5 years), coli surface antigen 2 (92%, 6-12 years; 83%, 2-5 years), and coli surface antigen 4 (93%, 6-12 years). Vaccination evoked a .gtoreq.4-fold rise in antitoxic IgA and IgG titers in 93% and 81% of children, respectively. In conclusion, the oral ETEC vaccine was safe and immunogenic in 2- to 12-year-old children, justifying further evaluation in infants.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:48:10 ON 03 DEC 2002)

- Author(s)

L27	138	SEA ABB=ON PLU=ON	"LANGERMANN S"?/AU
L28	113	SEA ABB=ON PLU=ON	"REVEL A"?/AU
L29	73	SEA ABB=ON PLU=ON	"AUGUSTE C"?/AU
L30	69	SEA ABB=ON PLU=ON	"BURLEIN J"?/AU
L31	3	SEA ABB=ON PLU=ON	L27 AND L28 AND L29 AND L30
L32	26	SEA ABB=ON PLU=ON	L27 AND (L28 OR L29 OR L30)
L33	3	SEA ABB=ON PLU=ON	L28 AND (L29 OR L30)
L34	10	SEA ABB=ON PLU=ON	L29 AND L30
L35	43	SEA ABB=ON PLU=ON	(L32 OR L27 OR L28 OR L29 OR L30) AND ADHESIN
L36	41	SEA ABB=ON PLU=ON	L35 AND (INFECTION OR ENTEROBACTER? OR ENTERO(W)(BACTER? OR BACILL?) OR ENTEROBACILLUS OR UTI)
L37	41	SEA ABB=ON PLU=ON	L31 OR L33 OR L34 OR L36
L38	17	DUP REM L37	(24 DUPLICATES REMOVED)

L38 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 2002:157597 HCAPLUS
DOCUMENT NUMBER: 136:215390
TITLE: FimH protein and FimH-FimC complex as vaccine for urogenital tract **infections**
INVENTOR(S): **Langermann, Solomon;** Ballou, W. Ripley
PATENT ASSIGNEE(S): Medimmune, Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015928	A1	20020228	WO 2000-US32398	20001128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001018049	A5	20020304	AU 2001-18049	20001128

PRIORITY APPLN. INFO.: US 2000-226146P P 20000818
WO 2000-US32398 W 20001128

AB The present invention relates to methods of stimulating an immune response in a primate utilizing compns. comprising bacterial **adhesin** proteins and/or immunogenic fragments thereof. The compns. are useful for the prevention and treatment of bacterial induced diseases involving bacterial adherence to a target cell, such as diseases of the urinary tract. More specifically, the invention relates to the vaccination of primates, preferably humans, with protein complexes, such as a purified FimH polypeptides, a purified FimC-FimH (FimCH) polypeptide complex, or immunogenic

fragments thereof, to stimulate protective immunity in the recipient against **infection** by pathogenic bacteria, including all types of **Enterobacteriaceae**, preferably Escherichia coli to produce specific immunoglobin mols. in the serum and urine or mucosal secretions of the subject.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:51508 HCAPLUS
DOCUMENT NUMBER: 136:117368
TITLE: FimH **adhesins** of Escherichia coli for therapy of urinary tract **infections**
INVENTOR(S): **Langermann, Solomon; Revel, Andrew; Auguste, Christine; Burlein, Jeanne**
PATENT ASSIGNEE(S): Medimmune, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004496	A2	20020117	WO 2001-US21525	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002150587	A1	20021017	US 2001-900575	20010706

PRIORITY APPLN. INFO.: US 2000-216750P P 20000707

AB The authors disclose the sequence characterization and recombinant expression of variants of the E. coli FimH protein. A plasmid-based method of producing FimH **adhesins** and FimC-FimH complexes are also disclosed. The recombinant **adhesins** are suggested for vaccination against urinary tract **infections**

L38 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:505237 HCAPLUS
DOCUMENT NUMBER: 137:62166
TITLE: Engineered pilus proteins for vaccination and immunotherapy
INVENTOR(S): Hultgren, Scott J.; **Langermann, Solomon**; Sauer, Frederic G.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002086037	A1	20020704	US 2001-27350	20011228
WO 2002059156	A2	20020801	WO 2001-US51037	20011220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-257880P P 20001222

AB The authors disclose construction of pilus proteins exhibiting structural stabilization. Stabilization is achieved by occupation of the subunit-binding site by a covalently attached N-terminal extension domain or non-covalently by an engineered chaperone or other pilus protein. Such extension provides a "donor strand complementary" segment which may be altered to attach an auxiliary portion.

L38 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2002:435308 HCAPLUS
DOCUMENT NUMBER: 137:138428
TITLE: Structural basis of tropism of Escherichia coli to the bladder during urinary tract **infection**
AUTHOR(S): Hung, Chia-Suei; Bouckaert, Julie; Hung, Danielle; Pinkner, Jerome; Widberg, Charlotte; DeFusco, Anthony; **Auguste, C. Gale**; Strouse, Robert; **Langermann, Solomon**; Waksman, Gabriel; Hultgren, Scott J.
CORPORATE SOURCE: Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Molecular Microbiology (2002), 44(4), 903-915
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The first step in the colonization of the human urinary tract by pathogenic Escherichia coli is the mannose-sensitive binding of FimH, the **adhesin** present at the tip of type 1 pili, to the bladder epithelium. We elucidated crystallog. the interactions of FimH with D-mannose. The unique site binding pocket occupied by D-mannose was probed using site-directed mutagenesis. All but one of the mutants examd. had greatly diminished mannose-binding activity and had also lost the ability to bind human bladder cells. The binding activity of the monosaccharide D-mannose was delineated from this of mannotriose (Man(.alpha.1-3)[Man(.alpha.1-6)]Man) by

generating mutants that abolished D-mannose binding but retained mannotriose binding activity. Our structure/function anal. demonstrated that the binding of the monosaccharide .alpha.-D-mannose is the primary bladder cell receptor for uropathogenic E. coli and that this event requires a highly conserved FimH binding pocket. The residues in the FimH mannose-binding pocket were sequenced and found to be invariant in over 200 uropathogenic strains of E. coli. Only enterohemorrhagic E. coli (EHEC) possess a sequence variation within the mannose-binding pocket of FimH, suggesting a naturally occurring mechanism of attenuation in EHEC bacteria that would prevent them from being targeted to the urinary tract.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:570883 BIOSIS
DOCUMENT NUMBER: PREV200200570883
TITLE: Structural basis of tropism of Escherichia coli to the bladder during urinary tract **infection**.
AUTHOR(S): Hung, C. (1); Bouckaert, J. (1); Hung, D. L. (1); Pinkner, J. (1); Widberg, C. (1); DeFusco, A.; Auguste, G.; Strouse, R.; **Langermann, S.**; Hultgren, S. J. (1)
CORPORATE SOURCE: (1) Medical School, Washington University, Saint Louis, MO USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 41. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 102nd General Meeting of the American Society for Microbiology Salt Lake City, UT, USA May 19-23, 2002 American Society for Microbiology . ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The first step in the colonization of the human urinary tract by pathogenic Esherichia coli is mediated by mannose-sensitive binding of FimH, the **adhesin** present at the tip of type 1 pili. We elucidated crystallographically the interactions of FimH with D-mannopyranoside. The unique site where bound D-mannose was observed was probed using site-directed mutagenesis. All mutants but one examined had greatly diminished mannose binding activity and had also lost the ability to bind human bladder cells. Two mutants were impaired and unable to colonize the bladder, but were able to bind with high affinity to mannotriose (Man(a1-3) (Man(a1-6))Man). Thus, mannose and not mannotriose is the primary bladder cell receptor for uropathogenic E. coli. The direct correlation of the mannose binding specificity of FimH with the pathogenesis caused by E. coli in the human bladder is confirmed in a strict conservation of the residues in the mannose binding pocket among FimH **adhesins** we sequenced from over 200 strains of E. coli. Only enterohemorrhagic E. coli (EHEC) possess a sequence variation within the mannose binding pocket of FimH.

L38 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 2001:64163 HCAPLUS

DOCUMENT NUMBER: 134:130261
TITLE: Escherichia coli FimH **adhesin** peptides and fusion proteins, and their use as vaccines for preventing diseases such as urinary tract **infection**
INVENTOR(S): Hultgren, Scott J.; **Langermann, Solomon**
PATENT ASSIGNEE(S): Medimmune, Inc., USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005978	A1	20010125	WO 2000-US19402	20000714
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194563	A1	20020410	EP 2000-950385	20000714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-144016P P 19990715
WO 2000-US19402 W 20000714

AB The invention provides immunogenic polypeptides comprising one or more domains of the Escherichia coli gene fimH **adhesin** protein, wherein the domains include mannose-binding (MBD) or collagen-binding (COL) domains. Five specific FimH polypeptides are provided including: (1) MBD-1, MBD-2 and MBD-3, which contain mannose-binding domains; (2) COL, which contains the collagen-binding domain, and (3) MBD-C which contains mannose and collagen binding domains. The invention also provides immunogenic FimH fusion proteins comprising said polypeptides sepd. by a linker peptide contg. glycine and serine amino acids. The invention specifically provides three fusion proteins including: (1) MBD-1-MBD-2-MBD-3; (2) MBD-1-MBD-C-MBD-3 and (3) MBD-1-MBD-2-COL-MBD-3. The invention further provides: (1) polynucleotides encoding the various FimH domains; (2) monoclonal antibodies specific for the said FimH polypeptides and fusion proteins; and (3) compn. comprising said monoclonal antibody. Still further, the invention provides for the use of said FimH polypeptides and fusion proteins as vaccines for preventing diseases caused by E. coli in humans, such as urinary tract **infection** . The amino acid sequences of E. coli MBD-1, MBD-2 and MBD-3 peptides are provided. The invention also included amino acid sequences of the fusion proteins claimed.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:227518 BIOSIS
DOCUMENT NUMBER: PREV200100227518
TITLE: Development of an **adhesin** vaccine to prevent urinary tract **infection**.
AUTHOR(S): Mulvey, Matthew A. (1); Hultgren, Scott J.; **Langermann, Solomon**
CORPORATE SOURCE: (1) Dept. Molecular Microbiology, Washington Univ. School Medicine, 660 S. Euclid Ave., St. Louis, MO, 63110-1093 USA
SOURCE: Lohner, Karl. (2001) pp. 123-137. Development of novel antimicrobial agents: Emerging strategies. print.
Publisher: Horizon Scientific Press Wymondham, Norfolk, NR18 0EH, UK.
ISBN: 1-898486-23-9 (cloth).
DOCUMENT TYPE: Book
LANGUAGE: English
SUMMARY LANGUAGE: English

L38 ANSWER 8 OF 17 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001547391 MEDLINE
DOCUMENT NUMBER: 21478204 PubMed ID: 11593791
TITLE: [Candidate vaccine against urinary tract **infections**].
Vaccin tegen urineweginfecties in ontwikkeling.
AUTHOR: Hoepelman I M; Meiland R; **Langermann S**
CORPORATE SOURCE: Universitair Medisch Centrum Utrecht (UMCU), afd. Acute Geneeskunde & Infectieziekten, Postbus 85.500, 3508 GA Utrecht.. i.m.hoepelman@digd.azu.nl
SOURCE: NEDERLANDS TIJDSCHRIFT VOOR GENEESKUNDE, (2001 Sep 22) 145 (38) 1860-2. Ref: 9
Journal code: 0400770. ISSN: 0028-2162.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Dutch
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20020122
Entered Medline: 20011204

AB Urinary tract **infections** (**UTIs**) are an important medical problem for women. The most common uropathogen is Escherichia coli. The adherence of E. coli to the uroepithelium is mediated by the FimH **adhesin**, a minor component of type-1 fimbriae. This is the initial step in the pathogenesis of **UTIs**. Recently, a candidate vaccine has been developed, based on this FimH **adhesin**. In animal studies and in a phase 1 study, this vaccine has proven to be both immunogenic and safe. In this era of increasing resistance to antibiotics, such a method of prevention is of high importance.

L38 ANSWER 9 OF 17 MEDLINE
ACCESSION NUMBER: 2001184845 MEDLINE
DOCUMENT NUMBER: 21103354 PubMed ID: 11171023
TITLE: Vaccination utilizing the FimCH complex as a strategy to prevent Escherichia coli urinary tract

infections.

AUTHOR: **Langermann S**; Ballou W R Jr
CORPORATE SOURCE: MedImmune, Inc., 35 W. Watkins Mill Rd., Gaithersburg, MD 20878, USA..
langermanns@medimmune.com
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (2001 Mar 1) 183 Suppl 1 S84-6. Ref: 13
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

L38 ANSWER 10 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:458890 BIOSIS
DOCUMENT NUMBER: PREV200100458890
TITLE: FimCH vaccine for prevention of Escherichia coli urinary tract **infections**.
AUTHOR(S): **Langermann, S. (1)**
CORPORATE SOURCE: (1) MedImmune, Inc., Gaithersburg, MD USA
SOURCE: International Journal of Antimicrobial Agents, (June, 2001) Vol. 17, No. Supplement 1, pp. S58. print.
Meeting Info.: 22nd International Congress of Chemotherapy Amsterdam, Netherlands June 30-July 03, 2001
ISSN: 0924-8579.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L38 ANSWER 11 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000134617 MEDLINE
DOCUMENT NUMBER: 20134617 PubMed ID: 10669375
TITLE: Vaccination with FimH **adhesin** protects cynomolgus monkeys from colonization and **infection** by uropathogenic Escherichia coli.
AUTHOR: **Langermann S**; Mollby R; **Burlein J E**; Palaszynski S R; **Auguste C G**; DeFusco A; Strouse R; Schenerman M A; Hultgren S J; Pinkner J S; Winberg J; Guldevall L; Soderhall M; Ishikawa K; Normark S; Koenig S
CORPORATE SOURCE: MedImmune, Inc., Gaithersburg, MD 20878, USA.
langermanns@medimmune. com.
CONTRACT NUMBER: AI-29549 (NIAID)
DK-51406 (NIDDK)
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (2000 Feb) 181 (2) 774-8.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000413

AB Escherichia coli FimH **adhesin** mediates binding to the bladder mucosa. In mice, a FimH vaccine protects against bacterial challenge. In this study, 4 monkeys were inoculated with 100 microgram of FimCH **adhesin**-chaperone complex mixed with MF59 adjuvant, and 4 monkeys were given adjuvant only intramuscularly. After 2 doses (day 0 and week 4), a booster at 48 weeks elicited a strong IgG antibody response to FimH in the vaccinated monkeys. All 8 monkeys were challenged with 1 mL of 108 E. coli cystitis isolate NU14. Three of the 4 vaccinated monkeys were protected from bacteruria and pyuria; all control monkeys were infected. These findings suggest that a vaccine based on the FimH **adhesin** of E. coli type 1 pili may have utility in preventing cystitis in humans.

L38 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 1999:525486 HCAPLUS
DOCUMENT NUMBER: 131:268633
TITLE: X-ray structure of the FimC-FimH chaperone-**adhesin** complex from uropathogenic Escherichia coli
AUTHOR(S): Choudhury, Devapriya; Thompson, Andrew; Stojanoff, Vivian; **Langermann, Solomon**; Pinkner, Jerome; Hultgren, Scott J.; Knight, Stefan D.
CORPORATE SOURCE: Dep. Molecular Biology, Uppsala Biomedical Center, Swedish Univ. Agricultural Sciences, Uppsala, S-753 24, Swed.
SOURCE: Science (Washington, D. C.) (1999), 285(5430), 1061-1066
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Type 1 pili-adhesive fibers expressed in most members of the **Enterobacteriaceae** family-mediate binding to mannose receptors on host cells through the FimH **adhesin**. Pilus biogenesis proceeds by way of the chaperone/usher pathway. The x-ray structure of the FimC-FimH chaperone-**adhesin** complex from uropathogenic Escherichia coli at 2.5 angstrom resoln. reveals the basis for carbohydrate recognition and for pilus assembly. The carboxyl-terminal pilin domain of FimH has an Ig-like fold, except that the seventh strand is missing, leaving part of the hydrophobic core exposed. A donor strand complementation mechanism in which the chaperone donates a strand to complete the pilin domain explains the basis for both chaperone function and pilus biogenesis.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1999:415405 HCAPLUS
DOCUMENT NUMBER: 131:241574
TITLE: **Adhesins** as targets for vaccine

development
AUTHOR(S): Wizemann, Theresa M.; Adamou, John E.; **Langermann, Solomon**
CORPORATE SOURCE: MedImmune, Inc., Gaithersburg, MD, 20878, USA
SOURCE: Emerging Infectious Diseases (1999), 5(3), 395-403
CODEN: EIDIFA; ISSN: 1080-6040
PUBLISHER: National Center for Infectious Diseases, Centers for Disease Control and Prevention
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 66 refs. Blocking the primary stages of **infection**, namely bacterial attachment to host cell receptors and colonization of the mucosal surface, may be the most effective strategy to prevent bacterial **infections**. Bacterial attachment usually involves an interaction between a bacterial surface protein called an **adhesin** and the host cell receptor. Recent preclin. vaccine studies with the FimH **adhesin** (derived from uropathogenic Escherichia coli) have confirmed that antibodies elicited against an **adhesin** can impede colonization, block **infection**, and prevent disease. The studies indicate that prophylactic vaccination with **adhesins** can block bacterial **infections**. With recent advances in the identification, characterization, and isolation of other **adhesins**, similar approaches are being explored to prevent **infections**, from otitis media and dental caries to pneumonia and sepsis.
REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 14 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:281585 BIOSIS
DOCUMENT NUMBER: PREV199800281585
TITLE: Systemic immunization with conserved pilus-associated **adhesins** protects against mucosal **infections**.
AUTHOR(S): Palaszynski, S.; Pinkner, J.; Leath, S.; Barren, P.; **Auguste, C. G.; Burlein, J.**; Hultgren, S.; **Langermann, S. (1)**
CORPORATE SOURCE: (1) Dep. Mucosal Immunity and Vaccines, MedImmune Inc., 35 West Watkins Mill Road, Gaithersburg, MD 20878 USA
SOURCE: Brown, F. [Editor]; Haaheim, L. R. [Editor]. Developments in Biological Standardization, (1998) Vol. 92, pp. 117-122. Developments in Biological Standardization; Modulation of the immune response to vaccine antigens.
Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland.
Meeting Info.: Symposium Bergen, Norway June 18-21, 1996 International Association of Biological Standardization
. ISSN: 0301-5149. ISBN: 3-8055-6640-9.
DOCUMENT TYPE: Book; Conference
LANGUAGE: English

L38 ANSWER 15 OF 17 MEDLINE DUPLICATE 9

Searcher : Shears 308-4994

ACCESSION NUMBER: 1998214883 MEDLINE
DOCUMENT NUMBER: 98214883 PubMed ID: 9554264
TITLE: Systemic immunization with conserved pilus-associated **adhesins** protects against mucosal **infections**.
AUTHOR: Palaszynski S; Pinkner J; Leath S; Barren P; **Auguste C G; Burlein J**; Hultgren S; **Langermann S**
CORPORATE SOURCE: Department of Mucosal Immunity and Vaccines, MedImmune, Inc., Gaithersburg, MD, USA.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1998) 92 117-22.
Journal code: 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB Colonization and **infection** of the bladder mucosa by Escherichia coli, the major uropathogenic organism, is dependent on the expression of pilus organelles. Type 1 pili are expressed by the majority of E. coli strains derived from patients with cystitis and pyelonephritis. FimH is the **adhesin** protein located at the distal tip of the heteropolymeric type-1 pilus which mediates binding to bladder cells through mannose receptors. We have shown that humoral antibody raised against two forms of purified FimH **adhesin** inhibited 94% (49/52) of E. coli **UTI** clinical isolates from binding to bladder tissue in vitro. Animals immunized with FimH-containing vaccines by a systemic route reduced colonization of the bladder mucosa in vivo in a murine cystitis model by > 99%. IgG antibody to FimH was detected in urinary samples obtained from immunized, protected mice. Passive systemic administration of immune sera from FimH-inoculated mice to naive animals also resulted in reduced colonization of bladder mucosa by uropathogenic E. coli. These studies demonstrate that systemic immunization with an anti-bacterial vaccine targeting a highly conserved **adhesin** on uropathogenic E. coli can induce IgG-mediated protection at a mucosal surface and may be a means of preventing recurrent and acute **infections** of the urogenital tract mucosa.

L38 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1997:286117 HCAPLUS
DOCUMENT NUMBER: 126:342180
TITLE: Prevention of mucosal Escherichia coli **infection** by FimH-**adhesin** -based systemic vaccination
AUTHOR(S): **Langermann, Solomon**; Palaszynski, Susan; Barnhart, Michelle; Auguste, Gale; Pinkner, Jerome S.; **Burlein, Jeanne**; Barren, Philip; Koenig, Scott; Leath, Simon; Jones, C. Hal; Hultgren, Scott J.
CORPORATE SOURCE: MedImmune, Inc., Gaithersburg, MD, 20878, USA
SOURCE: Science (Washington, D. C.) (1997), 276(5312), 607-611

Searcher : Shears 308-4994

PUBLISHER: CODEN: SCIEAS; ISSN: 0036-8075
American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Virtually all uropathogenic strains of Escherichia coli, the primary cause of cystitis, assemble adhesive surface organelles called type 1 pili that contain the FimH **adhesin**. Sera from animals vaccinated with candidate FimH vaccines inhibited uropathogenic E. coli from binding to human bladder cells in vitro. Immunization with FimH reduced in vivo colonization of the bladder mucosa by >99% in a murine cystitis model, and IgG to FimH was detected in urinary samples from protected mice. Furthermore, passive systemic administration of immune sera to FimH also resulted in reduced bladder colonization by uropathogenic E. coli. This approach may represent a means of preventing recurrent and acute **infections** of the urogenital mucosa.

L38 ANSWER 17 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:282007 BIOSIS
DOCUMENT NUMBER: PREV199799581210

TITLE: Effectiveness of a FimH-based vaccine against a large panel of diverse Escherichia coli clinical isolates.

AUTHOR(S): **Burlein, J. E.**; **Auguste, C. G.**; **Revel, A. T.**; Barren, P.; **Langermann, S.**
CORPORATE SOURCE: MedImmune Inc., Gaithersburg, MD USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1997) Vol. 97, No. 0, pp. 76.
Meeting Info.: 97th General Meeting of the American Society for Microbiology Miami Beach, Florida, USA May 4-8, 1997
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

FILE 'HOME' ENTERED AT 15:51:52 ON 03 DEC 2002

FILE 'HCAPLUS' ENTERED AT 12:31:19 ON 04 DEC 2002
L1 60 S (ENTEROBACTER? OR ENTERO BACTER?)(W)INFECT?
L2 2 S L1 AND ADHESIN

- Key terms

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:32:06 ON 04 DEC 2002
L3 27 S L2
L4 2 S L3 AND ADMIN?
L5 2 DUP REM L4 (0 DUPLICATES REMOVED)

L5 ANSWER 1 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002049267 EMBASE
TITLE: Protection of suckling neonatal pigs against infection with an enterotoxigenic Escherichia coli expressing 987P fimbriae by the **administration** of a bacterial competitive exclusion culture.
AUTHOR: Genovese K.J.; Harvey R.B.; Anderson R.C.; Nisbet D.J.
CORPORATE SOURCE: K.J. Genovese, USDA-ARS-SPARC, 2881 F and B Road, College Station, TX 77845, United States. genovese@ffsru.tamu.edu
SOURCE: Microbial Ecology in Health and Disease, (2001) 13/4 (223-228).
Refs: 25
ISSN: 0891-060X CODEN: MEHDE6
COUNTRY: Norway
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
046 Environmental Health and Pollution Control
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The objective of these experiments was to evaluate the effects of a porcine-derived CE culture, RPCF, on an enterotoxigenic Escherichia coli infection in suckling neonatal pigs. Litters of piglets from 18 crossbred sows were included in the study. All piglets remained on-sow for the duration of these studies. Piglets in RPCF groups were orally **administered** 5 ml of the RPCF bacterial competitive exclusion culture within 12 h of birth. Control piglets were given sterile medium orally as a placebo within 12 h of birth. At 48 h of age, piglets in all groups were orally challenged with an enterotoxigenic E. coli expressing the 987P fimbrial **adhesin**. Daily rectal swabs were taken, mortalities were recorded, and at 5 days post-challenge, piglets in all groups were euthanized and necropsied. Samples were taken from the ileum, jejunum, ileocecal junction, cecum, colon, and ileocecal lymph nodes and cultured for the presence and enumeration of E. coli. Significant reductions ($p < 0.001$) were observed in all samples taken at necropsy from RPCF-treated pigs when compared with control pigs. Both ileal and cecal concentrations of E. coli were reduced by 5 log(10) in those pigs that were **administered** the RPCF culture. A significant reduction in mortality was observed, decreasing from 23% in the control group to 2.7% in the RPCF group ($p < 0.001$). Clinical colibacillosis is a major economic and animal health concern in the swine industry. The RPCF CE culture may represent a means of possibly reducing the losses and morbidity associated with colibacillosis in pigs and, thus, may help to reduce the economic and animal health strains placed on the swine industry and the

animals therein.

L5 ANSWER 2 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999021809 EMBASE

TITLE: Oral, inactivated, whole cell enterotoxigenic Escherichia coli plus cholera toxin B subunit vaccine: Results of the initial evaluation in children.

AUTHOR: Savarino S.J.; Hall E.R.; Bassily S.; Brown F.M.; Youssef F.; Wierzba T.F.; Peruski L.; El-Masry N.A.; Safwat M.; Rao M.; El Mohamady H.; Abu-Elyazeed R.; Naficy A.; Svennerholm A.-M.; Jertborn M.; Lee Y.J.; Clemens J.D.

CORPORATE SOURCE: Dr. S.J. Savarino, c/o Research Publications Office, US Naval Medical Research Unit No. 3, Box 5000, FPO, AE 09835-0007, United States. savarino@namru.navy.mil

SOURCE: Journal of Infectious Diseases, (1999) 179/1 (107-114).
Refs: 38
ISSN: 0022-1899 CODEN: JIDIAQ

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English

AB Two randomized, double-blinded trials assessed the safety and immunogenicity of an oral, killed enterotoxigenic Escherichia coli (ETEC) plus cholera toxin B subunit vaccine in Egyptian children. Two doses of vaccine or E. coli K-12 were given 2 weeks apart to 105 6- to 12-year-olds and 97 2- to 5-year-olds. Safety was monitored for 3 days after each dose. Blood was collected before immunization and 7 days after each dose to measure immune responses. Few children reported postdosing symptoms, with no differences in the frequency of symptoms between treatment groups. Most vaccinees had an IgA antibody-secreting cell response against colonization factor antigen I (100%, 6-12 years; 95%, 2-5 years), coli surface antigen 2 (92%, 6-12 years; 83%, 2-5 years), and coli surface antigen 4 (93%, 6-12 years). Vaccination evoked a .gtoreq.4-fold rise in antitoxic IgA and IgG titers in 93% and 81% of children, respectively. In conclusion, the oral ETEC vaccine was safe and immunogenic in 2- to 12-year-old children, justifying further evaluation in infants.

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